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JOSEPH LISTER
As he appeared in 1895, aged 68

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NO. I



Joseph Lister

BIOGRAPHY

- 1827 Born April 5, son of Joseph Jackson and Isabella (Harris) Lister. Had three brothers and two sisters. His father was a Quaker and a wine merchant whose hobby was the study of optics and the making of lenses. Although largely self-taught he was given a fellowship in the Royal Society in 1832. Joseph Lister attended school at Hitchen and at Grove House, Tottenham. He was a precocious boy, read the Latin classics and wrote several papers on natural history.
- 1844 Age 17. Entered University College, London, because it had no religious requirements or affiliations. After 3 years he received the degree of A.B.
- 1848 Age 21. Began study of medicine. Anesthetics were just being introduced.
- 1852 Age 25. Given the degree of M.B. at the University of London and a Fellowship of the Royal Society of Surgeons.
- 1853 Age 26. Lister was advised by his teacher William Sharpey to visit several medical centers, among them Edinburgh. In the latter city, Lister was cordially received by Syme, the leading surgeon of Britain, and given work in Syme's wards.
- 1854 Age 27. Lister became assistant surgeon in the Infirmary and was busy in teaching.
- 1856 Age 29. Lister married Syme's daughter, Agnes, after resigning from the Quakers and becoming a member

of the Church of England. After a honeymoon of three months spent in travel on the continent where Lister met the leading medical men of his time, he began practice in Edinburgh.

- 1860 Age 33. Appointed professor of surgery in the University of Glasgow.
- 1861 Age 34. Became surgeon to the Royal Infirmary.
- 1865 Age 38. While studying suppuration, became acquainted with Pasteur's work on putrefaction.
- 1867 Age 40. Wrote first articles on antiseptic treatment of wounds.
- 1869 Age 42. Elected professor of surgery at Edinburgh when Syme resigned because of poor health. Reduced his lectures to two a week, often had 170 students in a class. Continued work on antiseptic methods.
- 1875 Age 48. Traveled extensively in Europe.
- 1876 Age 49. Visited the United States and was made President of the Surgical Section of the International Medical Congress in Philadelphia.
- 1877 Age 50. Accepted newly created chair of clinical surgery at King's College, London.
- 1878 Age 51. A juror at the University Exhibition at Paris.
- 1883 Age 56. Made a Baronet.
- 1891 Age 64. Instrumental in establishing the British Institute for Preventive Medicine (later re-named after Lister).
- 1892. Age 65. Retired from his professorship at King's College.
- 1893. Age 66. Lady Lister died of pneumonia while traveling in Italy. They had no children.
- 1895 Age 68. Elected President of the Royal Society.
- 1897 Age 70. Again traveled widely in the United States and Canada. Was elevated to the peerage.
- 1909 Age 82. Sight and hearing became impaired, could neither read nor write.
- 1912 Age 85. Died on February 12. Following his wish, he was not buried in Westminster Abbey, but was interred beside his wife at the West Hampstead Cemetery.

"Lister was almost worshiped by his patients. He was so extremely sympathetic, so gracious in his manner, and so attentive to all their wants. His thoughtful face showed obvious mastery of himself and of his situation." P. F. Clark.

INTRODUCTION TO THE WRITINGS OF LISTER

Joseph Lister takes his place with Paré and John Hunter as the third of the three greatest surgeons of all time because of a fortunate series of circumstances.

Lister's father, Joseph Jackson Lister, although a wine merchant by trade, did a great amount of work in developing optical lenses. He taught his son the use of the microscope and developed in him an interest in objects of nature. From his father, also, Joseph inherited a love for the classics. At an early age he was able to read these classics in the original Latin and with his father's aid wrote several papers on subjects in natural history.

The second factor influencing the development of Joseph Lister was his attendance at medical school at the time when anesthesia was being introduced into surgery. Before the use of ether and chloroform the surgeon had to perform his operations in as short a time as possible. Minutes were as years to the patient. The surgeon could not do a careful, painstaking operation but had to work rapidly. After anesthesia, the next great step to be made was the control of infection. Most operations were followed by suppuration and discharge of pus. Those were the days of "laudable" pus when it was thought that a discharge of matter was necessary for the proper healing of wounds. Hippocrates and, several centuries later, Henri de Mondeville, had taught that healing without pus was desirable but their teaching had little influence. Perhaps many surgeons wished their patients to be without infection and pus formation, but since no one knew the cause of infection, no one knew how to prevent it.

A third factor in the development of Joseph Lister was his visit to several medical centers as soon as he had been graduated from medical school. His wise teacher, William Sharpey, ad-

vised this completion of his education. In Edinburgh Lister, then only twenty-six years of age, was cordially received by James Syme, at that time the leading surgeon of the British Isles. Lister became an assistant to Syme and two years later married his daughter.

From the very beginning of his residence in Edinburgh, Lister was engaged in research on inflammation, coagulation of blood and infection. He published several papers on these subjects. He found his hospital wards terribly affected with septicemia, pyemia, erysipelas and hospital gangrene. In 1866 his own cases of amputation had a mortality of 45 per cent.

In the course of his studies and eagerness to find a way to control infection, Lister came upon an article recently published by the famous scientist, Louis Pasteur. Pasteur had proven that there is no such thing as spontaneous generation and that all putrefaction is due to the growth of living organisms or bacteria. Lister at once recognized the value of applying Pasteur's discovery to human beings to prevent or control infection.

Because Pasteur's method of sterilization by heat could not be applied to living tissues, Lister sought a chemical which would prevent contamination of wounds by organisms in the air. He was acquainted with the problem of the village fathers of a nearby town, Carlyle, where the populace was aroused because of the odor of the local sewage disposal system. The town board of Carlyle had found that the addition of a small amount of carbolic acid to the sewage prevented putrefaction and thus abolished the odor. Lister determined to apply carbolic acid to his cases of compound fracture and thus, by preventing decomposition of the tissue, have primary union of the injured bone and lacerated tissues.

The story of his experiences in instituting this treatment and the results he obtained in his first cases is republished here. These papers of Lister thus inaugurated a new era in surgery, the antiseptic era. From this period there was a rapid development to the aseptic period in which, by mechanical and chemical means, everything which comes in contact with the patient's tissues at the time of operation is sterilized. No bacteria are

present to cause putrefaction and the horrors of surgery of Lister's day.

BIBLIOGRAPHY OF WRITINGS

1. Observations on the muscular tissue of the skin. 7 pp., 8°, Lond., W. Clowes & Sons, 1853.
2. Observations on the contractile tissues of the iris. Quart. J. Micr. Sc., Lond., 1: 3-11, 1853.
3. On a remarkable case of hydrocele. Edinb. M. J., 2: 236-239, 1856.
4. Case of pedunculated exostosis. Ibid., 2: 1034, 1857.
5. On the early stages of inflammation. Proc. Roy. Soc., Lond., 8: 581-587, 1851. Also: Edinb. M. J., 3: 656-660, 1858.
6. On the minute structure of involuntary muscular fibre. Tr. Roy. Soc. Edinb., 21: 549-557, 1857.
7. On spontaneous gangrene from arteritis and on the causes of coagulation of the blood in diseases of the blood-vessels. Edinb. M. J., 3: 893-907, 1858.
8. Further experiments on the coagulation of the blood. (Brief note) Ibid., 3: 1049-1050, 1858.
9. Case of ligature of the brachial artery, illustrating the persistent vitality of the tissues. Ibid., 4: 119-120, 1858.
10. Example of mixed aortic aneurism. Case. Ibid., 4: 546, 1858.
11. Preliminary account of an inquiry into the function of the visceral nerves, with special reference to the so-called inhibitory system. Proc. Roy. Sc. Lond., 9: 367-380, 1858.
12. Contributions to physiology and pathology; an inquiry regarding the parts of the nervous system which regulate the contractions of the arteries; On the cutaneous pigimentary system of the frog; On the early stages of inflammation. Phil. Trans. 148: 607-625; 627-643; 645-701, 1858.
13. Observations on the structure of nerve-fibers. With William Turner. Quart. J. Micr. Sc., Lond., 8: 3-8, 1859.

14. Case of amputation of leg (railway accident). Exhibition of needle to facilitate application of silver wire sutures. *Edinb. M. J.*, 4: 952-954, 1859.
15. Notice of further researches on coagulation of blood. *Ibid.*, 5: 536-40, 1859. Also: *Proc. Roy. Soc., Lond.*, 12: 580-611, 1862-63. Also: *Lancet*, 35: 281-91, 1864.
16. Excision of wrist for caries. *Lancet*, 1: 306-316, 1865.
17. On a new method of treating compound fractures, abscess, etc., with observation on the condition of suppuration. *Lancet*, 1: 326-329; 357-359; 387-389; 507-509; 2: 95-96, 1867. Also: *London Lancet*, 1: 364-373; 418; 622-624, 1867. Also, in German: *Klassiker der Medizin*, vol. 17, Leipzig, J. A. Barth, 1912.
18. On the antiseptic principle in the practice of surgery. *Brit. M. J.*, 2: 246-248, 1867. Also: *Lancet*, 2: 353-668, 1867. Also: *London Lancet*, 1: 741-745, 1867. Also in: *Epoch-Making Contributions to Medicine*, by C. N. B. Camac, pp. 9-20, Phila., Saunders, 1909. Also, in German: *Klassiker der Medizin*, vol. 17, Leipzig, J. A. Barth, 1912.
19. Contribution to antiseptic treatment in surgery; an address. *Brit. M. J.*, 2: 53-56; 101-102; 461-463; 515-517, 1868; 1: 301-304, 1869. Also, in German: *Klassiker der Medizin*, vol. 17, Leipzig, J. A. Barth, 1912.
20. Illustrations of the antiseptic system of treatment in surgery. *Lancet*, 1: 92-94, 1868.
21. Observations on ligature of arteries on the antiseptic system. *Lancet*, 40: 289-295, 1869.
22. Introductory lecture delivered in the University of Edinburgh, Nov. 8, 1869. 22 pp., 8°, Edinburgh, Edmontson & Douglas, 1869.
23. On the effects of the antiseptic system of treatment upon the salubrity of a surgical hospital. *London Lancet*, 1: 194-200, 1870.
24. Remarks on a case of compound dislocation of the ankle with other injuries, illustrating the antiseptic system of treatment. *Ibid.*, 360-368, 1870.
25. The Glasgow infirmary and the antiseptic treatment. *Lancet*, 1: 210-211, 1870.

26. Further evidence regarding effects of the antiseptic treatment upon the salubrity of a surgical hospital. *Ibid.*, 287-289, 1870.
27. A method of antiseptic treatment applicable to wounded soldiers in the present war. *Brit. M. J.*, Lond., 2: 243-244, 1870.
28. Case of dislocation of the hip-joint, downwards and inwards, reduced by manipulation. *Edinb. M. J.*, 16: 148, 1871.
29. Address in surgery (antiseptic treatment of wounds). *Brit. M. J.*, Lond., 2: 225-233, 1871. Also: *Jour. de Med., Chir. and Pharmacol.*, Brux., 53: 287; 407, 1871; 54: 33-46, 1872.
30. On some cases illustrating the results of excision of the wrist for caries, treatment of deformity from contracted cicatrix, and antiseptic dressing under circumstances of difficulty, including amputation at the hip-joint. *Edinb. M. J.*, 17: 144, 1872.
31. A contribution to the germ theory of putrefaction and other fermentative changes, and to the natural history of *Torulae* and bacteria. *Tr. Roy. Soc. Edinb.*, 27: 313-344, 1873.
32. A further contribution to the natural history of bacteria and the germ theory of fermentative changes. *Quart. J. Micr. Sc.*, Lond., n.s. 13, 1873.
33. On a case of rupture of the axillary artery in an attempt to reduce a dislocation of the shoulder. *Edinb. M. J.*, 18: 829-831, 1873.
34. Cases presented; omental hernia; tumor of femor; fibrous tumor; apparatus for producing an antiseptic spray. *Ibid.*, 20: 69-73, 1874.
35. Case of rodent ulcer. *Ibid.*, 268-270.
36. Cases in which antiseptics were used. *Ibid.*, 556-557.
37. Demonstration of antiseptic surgery before members of the British Medical Association in the operating theatre of the Royal Infirmary. *Ibid.*, 21: 193-205; 481-487, 1875.
38. *Principii et applicazione del metodo antisettico*. *Indipendente*, Torino, 26: 438-443, 1875.

39. On recent improvements in the details of antiseptic surgery. *Lancet*, 1: 365-367; 401-402; 434-436; 468-470; 603-605; 717-719; 787-789, 1875. Also: *London Lancet*, 1: 269-273; 319-327; 375-380, 1875.
40. Antiseptic surgery. *Trans. Internat. Med. Cong., Phila.*, pp. 535-544, 1876.
41. The antiseptic method of dressing open wounds. *Med. Rec.*, N. Y. 2: 695, 1876.
42. Graduation address at Edinburgh University. *Edinb. M. J.*, 22: 280-284, 1876.
43. Address in surgery. *Ibid.*, 464-467.
44. Sur la méthode antiseptique. *Bull. et mém. Soc. de chir. de Par.*, 4: 421-426, 1878.
45. Clinical lecture on a case of excision of the knee-joint and on horse-hair as a drain for wounds. *Lancet*, 1: 5-9, 1878.
46. A case of multiple papillomatous growths in the larynx, extirpated by complete laryngotomy; removal of the whole length of both true and false vocal cords; preservation of the voice; coexistence of thoracic aneurysm. With J. B. Yeo. *Tr. Clin. Soc., Lond.*, 11: 104-113, 1878. Also: *Med. Rec.*, N. Y., 16: 117, 1879.
47. A demonstration in antiseptic surgery. *Dublin Jour. Med. Soc.*, 3 s., 68: 97-114, 1879.
48. Excision of elbow-joint. *Case. Med. Times & Gaz.*, 1: 175, 1879.
49. Stricture; fistula in perineo; embolism of both limbs, *Ibid.*, 175, 1879.
50. Remarks on dressing. *Ibid.*, 2: 502, 1879.
51. Ueber antiseptische Wundbehandlung. *Allg. Wien. Med. Zeitg.*, 24: 395, 1879. Also: *Med.-Chir. Centralbl., Wien.*, 14: 578, 1879.
52. Mr. Syme's treatment of incised wounds. (Letter). *Lancet*, 1: 28-29, 1879.
53. Clinical lecture illustrating antiseptic surgery. *Lancet*, 2: 901-905, 1879. Also: *Boston M. & S. J.*, 102: 116; 140-142; 1880.

54. An address on the influence of position upon local circulation. *Brit. M. J.*, 1: 923-926, 1879.
55. Mr. Spence on surgical statistics. *Ibid.*, 1: 237-239; 276-278, 1880.
56. Gelatinous degeneration of knee-joint. *Med. Times & Gaz.*, 1: 579, 1880.
57. Lecture illustrating antiseptic surgery. *London Lancet*, 1: 493-500, 1880.
58. Remarks on microorganisms; their relation to disease. *Clin. News, Phila.*, 1: 469-472, 1880. Also: *Quart. J. Micr. Soc.*, n.s. 21: 330-342, 1881. Also: *Lancet*, 2: 695-698, 1881. Also: *London Lancet*, 1: 1-5, 1882. Also: *Wien. med. Bl.*, 4: 1385; 1420; 1449, 1881.
59. A series of cases of mammary diseases. *Brit. M. J.* 2: 777-779, 1881.
60. An address on the treatment of wounds. *Lancet*, 2: 863-866; 901-903, 1881.
61. President's address (on catgut ligature). *Tr. Clin. Soc., Lond.*, 14: xliii-lxiii. Also: *Lancet*, 1: 201-206; 275, 1881. Also: *Brit. M. J.*, 1: 183-185; 219-221, 1881. Also: *Berl. klin. Wochenschr.*, 18: 177; 194, 1881.
62. Gunshot wound of left forearm. *Med. Times & Gaz.*, 2: 660, 1882.
63. Sul trattamento delle ferite. Discorso pronunciato nella serione chirurgica del congresso medico internazionale al terminare della discussione sull' argomento—8 Agosto, 1881. Trad. dall'inglese del dott. Gregorio Fedeli. *Raccoglitore med.*, 1882. Also: Forli, tip. Democratica, 22 pp., 8°, 1882.
64. Chirurgie antiseptique et théorie des germes. *Oeuvres réunies de — Traduction du Dr. Gustave Borginon.* xvi, 5-635 pp., 8°, Paris, A. Delahaye & E. Lecrosnier, 1882.
65. An address on the treatment of fracture of the patella. *Brit. M. J.*, 2: 855-860, 1883.
66. An address on corrosive sublimate as a surgical dressing. *Lancet*, 2: 723-728, 1884. Also: *Brit. M. J.*, 2: 803-807, 1884. Also: *Wien. Med. Bl.*, 7: 1375; 1412; 1448, 1884.

67. An address on a new antiseptic dressing. *Brit. M. J.*, 2: 1025-1029, 1889. Also: *Illust. M. News*, 5: 125-127, 1889. Also: *Lancet*, 2: 943-947, 1889. Also: *Med. Rec.*, N. Y., 36: 561-566, 1889. Also: *Wien. Med. Bl.*, 12: 723; 741, 1889.
68. On two cases of long-standing dislocation of both shoulders treated by operation. *Lancet*, 1: 1, 1890. Also: *North. Lancet*, Winnipeg, 3: 155-161, 1889-90. Also, abstr.: *Tr. Hunter. Soc. Lond.*, pp. 91-94, 1889-90. Also: *Wien. Med. Bl.*, 13: 22; 38, 1890.
69. Further observations on the cyanide of zinc and mercury. *Lancet*, 1: 2-4, 1890. Also, abstr.: *Tr. Hunter. Soc. Lond.*, pp. 91-94, 1889-90.
70. On the present position of antiseptic surgery. In: *Wood's M. & S. Monographs*. N. Y. 8: 551-562, 1890. Also: *Verhandl. d. X. internat. med. Cong.*, 1890, Berl., 1: 28-35, 1891. Also: *Brit. M. J.* 2: 377-379, 1890.
71. Lectures on Koch's treatment of tuberculosis. *Lancet*, 2: 1257, 1890. Also: *Brit. M. J.*, 2: 1372-1374, 1890.
72. On the principles of antiseptic surgery. *Internat. Beitr. z. wissensch. Med. Festschr. R. Virchow* —, Berl., 3: 259-270, 1891.
73. On the coagulation of the blood in its practical aspects. *Brit. M. J.*, 1: 1057-1060, 1891. Also: *Med. Press. & Circ.*, n. s. 51: 449, 1891. Also: *Lancet*, 1: 1081-1084, 1891. Also: *Wien. Med. Bl.*, 14: 383; 398, 1891.
74. An address on the antiseptic management of wounds. *Brit. M. J.*, 1: 161-162; 277-278; 337-339, 1893. Also: *Lancet*, 1: 179-180; 285-286; 345-347, 1893. Also, in Italian: *Gazz. med. lomb.*, Milano, 52: 165; 263; 288; 297, 309; 324; 334; 348, 1893.
75. Presidential address on the relation of clinical medicine to modern scientific development. *Brit. M. J.*, 2: 733-741, 1896.
76. Address as president before British Association for Advancement of Science. *Science*, n. s. 4: 409-429, 1896.
77. *L'art de guérir et la science*. *Rev. scient.*, Par., 4 s., 6: 481-494, 1896.

78. An address on the value of pathological research. *Brit. M. J.*, 1: 317-319, 1897. Also: *Rev. scient., Par.*, 4 s. 7: 208-211, 1897.
79. Lord Lister on the vaccination question. *Abstr.: Lancet*, 2: 426-427, 1898.
80. The Huxley lecture; delivered to the Charing Cross Medical School, Oct. 2, 1900. *Brit. M. J.*, 2: 969-977, 1900.
81. On recent researches with regard to the parasitology of malaria. *Ibid.*, 2: 1625-1627, 1900. Also: *Wien. med. Presse*, 42: 729-736, 1901.
82. On early researches leading up to the antiseptic system of surgery. *Lancet*, 2: 985-993, 1900.
83. The third Huxley lecture; delivered before the Medical School of Charing Cross Hospital. *Lond., Harrison & Sons*, 58 pp., 8°, 1907.
84. Introduction to Stephen Paget's "Experiments on Animals." *N. Y., Wood*, 1907.
85. Note on the preparation of catgut for surgical purposes. *Brit. M. J.*, 1: 125-126, 1908. Also: *Lancet*, 1: 148-149, 1908.
86. Remarks on the treatment of fractures of the patella of long standing. *Brit. M. J.*, 1: 849-850, 1908. Also: *Lancet*, 1: 1049-1050, 1908.
87. Remarks on some points in the history of antiseptic surgery. *Brit. M. J.*, 1: 1557-1558, 1908. Also: *Lancet*, 1: 1815-1816, 1908.
88. On sulpho-chromic catgut. *Lancet*, 1: 273, 1909.
89. The collected papers of Joseph, Baron Lister. 2 vol., 4°, *Oxford, Clarendon Press*, xliv, 429 pp., 14 pl., vii, 489 pp., 4°, 1909.
90. Six papers by Lord Lister with a short biography and explanatory notes by Sir Rickman J. Godlee. vii, 194 pp., *Lond., J. Bale*, 1921.

BIBLIOGRAPHY OF BIOGRAPHIES

- Biography. *Méd. mod., Par.*, 7, suppl. 57, 1896.
Biography. *Nature, Lond.*, 54: 1-5, 1896.
Biography. *Canad. Pract., Toronto*, 22: 625-641, 1897.

- Biography. Pop. Sc. Month., N. Y., 52: 693-698, 1897-8.
- Lord Lister and his pupils. Brit. M. J., 1: 1374, 1897.
- Lord Lister and his work. By G. T. McKeough. Physician & Surg., Detroit, 20: 63-67, 1898.
- Lord Lister and his work. By A. Miles. Edinb. Health Soc., Health Lect., 15: 99-112, 1898-99.
- Lord Lister and the development of antiseptic surgery. By J. Finlayson. Janus, 5: 1: 57, 1900.
- Biography. N. Y. Med. J., 75: 1146, 1902.
- List of Lord Lister's contributions to medical and scientific literature down to the year 1897. By Chiene. Brit. M. J., 2: 1853, 1902.
- Lister jubilee number. Brit. M. J., 2: 1817-1861, 1902.
- Lister—jubilee, December 1902. By J. Berg. Hygiea, Stockholm, 2.f., 3: 282, 1903.
- Biography. By G. Hubert. Tidskr. f. d. norske Lægefor., Kristiania, 23: 347-359, 1903.
- A trip to England and some reminiscences of Lord Lister. By L. L. Hill. Mobile M. & S. J., 3: 487-494, 1903.
- Biography. By W. Thulstrup. Tidsskr. f. Jordemødre, København, 17: 101-109, 1906-7.
- Biography. By A. Martin & A. Rosthorn. Monatschr. f. Geburtsh. u. Gynäk., 25: 689-691, 1907.
- Biography. By J.P. zum Busch. München. med. Wochenschr., 54: 673-675, 1907.
- Lord Lister and the antiseptic method. Editorial. Lancet, 1: 1617-1620, 1909.
- Address on the presentation of a memorial of Lord Lister at the opening of the new Glasgow Royal Infirmary, June 23, 1909. By R. J. Godlee. Glasgow M. J., 72: 81-88, 1909.
- Lister prize essay; the life and work of Lister. By C. C. W. Judd. Johns Hopkins Hosp. Bull., 21: 293-304, 1910.
- Lister and his work. By C. M. Steele. Plexus, Chicago, 16: 449-466, 1910.
- Some personal reminiscences of Lord Lister. By L. L. Hill. Med. Rec., N. Y., 80: 327-329, 1911. Also: Tr. M. Ass. Alabama, pp. 316-322, 1911.

- Lister; his life and work. By A. A. Lendon. Australas. M. Gaz., 31: 261-264, 1912.
- Lord Lister. By N. A. Powell. Canada Lancet, 45: 655, 1911-12.
- Lister; an appreciation. By R. Roxburgh. Bristol M. Chir. J. 30: 1-10, 1912.
- Obituary. J. A. M. A., 58: 499, 1912.
- Obituary. N. Y. Med. J., 95: 342, 1912.
- Obituary. Brit. M. J., 1: 397-402, 1912.
- Obituary. Edinb. M. J., n.s. 8: 254-256, 1912.
- Obituary. Lancet, 1: 465-472, 1912.
- Obituary. Med. Press & Circ., n.s. 93: 117, 1912.
- Obituary. Am. Med., n.s. 7: 74-76, 1912.
- Obituary. Deutsche med. Wochenschr., 38, 1912.
- Obituary. Bio.-chem. Bull., N. Y., 1: 371, 1911-1912.
- Obituary. Glasgow M. J., 77: 190-196, 1912.
- Obituary. Med. Times, 40: 68, 1912.
- Biography. By E. Sonnenburg. Berl. klin. Wochenschr., 49: 485-487, 1912.
- Funeral. Brit. M. J., 1: 440-446, 1912.
- Biography. By J. Stewart. Canad. J. M. & S., 31: 323-330, 1912.
- Biography. By F. Trendelenburg. Deutsche med. Wochenschr., 38: 713-716, 1912.
- Biography. By E. Payr. Deutsche Zeitschr. f. Chir., 120: 1-6, 1912.
- Biography. By Hj. von Bonsdorff. Finska läk-sällsk. Landl., Helsingfors, 1: 343-347, 1912.
- Biography. B. J. Berg. Hygiea, Stockholm, 74: 257-264, 1912.
- Biography. By A. DePage. J. méd. de Brux., 17: 77, 1912.
- Biography. By J. Lucas-Championnière. J. de méd. et chir. prat., Par., 83: 129-135, 1912.
- Lord Lister and the era of modern surgery. By W. H. Seward. Albany M. Ann., 33: 449-451, 1912.
- Lister in London. By J. Stewart. Canada Lancet, 45: 661-664, 1911-12.

- Personal recollections of Lord Lister. By J. Stewart. *Canad. Pract. & Rev.*, 37: 270-277, 1912.
- Lord Lister; a tribute and an impression. By J. L. Waters. *Caledon. M. J.*, Glasg., 9: 59-65, 1912-13.
- Memorial address in appreciation of Baron Joseph Lister. By H. G. Wetherill & W. W. Grant. *Colorado Med.*, 9: 106-110, 1912.
- Biography. By A. Martin. *Monatschr. f. Geburtsch. u. Gynäk.*, 35: 265-267, 1912.
- Biography. By W. W. Cheyne. *Nature, Lond.*, 88: 556-560, 1912.
- Biography. By O. Lanz. *Nederl. Tijdschr. v. Geneesk.*, 1: 425-428, 1912.
- Biography. By J.-L. Faure. *Presse méd.*, 20: annexe, 185-187, 1912.
- Biography. By H. Caenen. *Zeitschr. f. d. ärztl. Fortbild.*, Jena, 9: 161-164, 1912.
- Personal reminiscences of Joseph Lister. By St. G. Baldwin. *Canad. J. M. & S.*, 31: 343-347, 1912. Also: *Canada Lancet*, 45: 672-674, 1911-12.
- Joseph Lister und seine Bedeutung für die Chirurgie. By E. Bäumer. *Deutsche med. Presse*, 16: 53, 1912.
- Surgical practice and its daily debt to Lister. By G. A. Bingham. *Canad. J. M. & S.*, 31: 348-350, 1912. Also, abstr.: *Canada Lancet*, 45: 668, 1911-12.
- Biography. By Sir W. Macewen. *Proc. Roy. Inst. Gr. Brit.*, 20: pt. 2: 546-564, 1912.
- Biography. By J. Lucas-Championnière. *Rev. de chir.*, Par., 45: 529-543, 1912.
- Biography. By J. Akermann. *Tidsskr. i mil. Hälsov.*, Stockholm, 37: 83-90, 1912.
- Biography. By V. Meisen. *Ugesk. f. Læger*, Kjöbenhavn., 74: 284-293, 1912.
- Biography. By F. C. Pybus. *Univ. Durham Coll. Med. Gaz.*, Newcastle, 13: 157-159, 1912-13.
- Biography. By F. H. Hancock. *Virginia M. Semi-Month.*, Richmond, 17: 15-20, 1912-13.

- Biography. By A. Fraenkel. *Wien. klin. Wochenschr.*, 25: 381-386, 1912.
- Biography. By Moszkowicz. *Wien. med. Wochenschr.*, 62: 509, 1912.
- Lister and the catgut ligature. By H. C. Cameron. *Brit. M. J.* 1:579, 1912.
- A memory and an appreciation of Lister. By H. C. Cameron. *Canad. J. M. & S.*, 31: 288-295, 1912. Also, abstr.: *Canada Lancet*, 45: 664-668, 1911-12.
- The influence of the researches of Pasteur and Lister on surgical pathology. By H. C. Cameron. *Canad. J. M. & S.*, 31: 311-322, 1912.
- Lister's work and teaching. By Sir W. W. Cheyne. *Clin. J. Lond.*, 41: 257-266, 1912-13. Also: *Tr. M. Soc., Lond.*, 36: 1-19, 1912-13.
- Lister, an appreciation. By J. B. Huber. *Am. Pract., N. Y.*, 46: 116-122, 1912.
- Persönliche Erinneurungen an Joseph Lister. By Madelung. *Strassb. med. Zeitg.*, 9: 55-60, 1912.
- Lister in Glasgow. By A. E. Malloch. *Canada Lancet*, 45: 656-658, 1911-12.
- Some memories of Mr. Lister. By A. E. Malloch. *Canad. J. M. & S.*, 31: 331-336, 1912.
- Personal reminiscences of Lister. By A. E. Malloch. *Canad. M. Ass. J.*, 2: 502-506, 1912.
- Joseph Lister in seiner Bedeutung für das Rettungswesen. By O. Marcus. *Zeitschr. f. Samariter-u. Rettungsw.*, Leipz., 18: 41, 1912.
- Personal reminiscences of Lord Lister. By H. A. Marcy. *Canada Lancet*, 45: 669-671, 1911-12.
- Personal reminiscences of Lord Lister; the introduction and development of antiseptic surgery in America. By H. A. Marcy. *Am. J. Surg.*, 26: 97-101, 1912.
- Reminiscences of the late Lord Lister. By R. H. Marten & W. T. Hayward. *Australas. M. Gaz.*, 31: 293-297, 1912.
- The funeral of Lord Lister. By Sir W. Osler. *Canad. M. Ass. J.*, 2: 343, 1912.

- Personal recollections of Lord Lister. By J. Stewart. *Canad. Pract. & Rev.*, 37: 270-277, 1912.
- Lord Lister; a tribute and an impression. By J. L. Waters. *Caledon. M. J., Glasg.*, 9: 59-65, 1912-13.
- Memorial address in appreciation of Baron Joseph Lister. By H. G. Wetherill & W. W. Grant. *Colorado Med.*, 9: 106-110, 1912.
- Biography. By A. Martin. *Monatschr. f. Geburtsch. u. Gynäk.*, 35: 265-267, 1912.
- Biography. By W. W. Cheyne. *Nature, Lond.*, 88: 556-560, 1912.
- Biography. By O. Lanz. *Nederl. Tijdschr. v. Geneesk.*, 1: 425-428, 1912.
- Biography. By J.-L. Faure. *Presse méd.*, 20: annexe, 185-187, 1912.
- Biography. By H. Caenen. *Zeitschr. f. d. ärztl. Fortbild.*, Jena, 9: 161-164, 1912.
- Personal reminiscences of Joseph Lister. By St. G. Baldwin. *Canad. J. M. & S.*, 31: 343-347, 1912. Also: *Canada Lancet*, 45: 672-674, 1911-12.
- Joseph Lister und seine Bedeutung für die Chirurgie. By E. Bäumer. *Deutsche med. Presse*, 16: 53, 1912.
- Surgical practice and its daily debt to Lister. By G. A. Bingham. *Canad. J. M. & S.*, 31: 348-350, 1912. Also, abstr.: *Canada Lancet*, 45: 668, 1911-12.
- Biography. By Sir W. Macewen. *Proc. Roy. Inst. Gr. Brit.*, 20: pt. 2: 546-564, 1912.
- Biography. By J. Lucas-Championnière. *Rev. de chir., Par.*, 45: 529-543, 1912.
- Biography. By J. Akermann. *Tidsskr. i mil. Hälsov.*, Stockholm, 37: 83-90, 1912.
- Biography. By V. Meisen. *Ugesk. f. Laeger, Kjöbenh.*, 74: 284-293, 1912.
- Biography. By F. C. Pybus. *Univ. Durham Coll. Med. Gaz.*, Newcastle, 13: 157-159, 1912-13.
- Biography. By F. H. Hancock. *Virginia M. Semi-Month.*, Richmond, 17: 15-20, 1912-13.

- Biography. By A. Fraenkel. *Wien. klin. Wochenschr.*, 25: 381-386, 1912.
- Biography. By Moszkowicz. *Wien. med. Wochenschr.*, 62: 509, 1912.
- Lister and the catgut ligature. By H. C. Cameron. *Brit. M. J.* 1:579, 1912.
- A memory and an appreciation of Lister. By H. C. Cameron. *Canad. J. M. & S.*, 31: 288-295, 1912. Also, *abstr.: Canada Lancet*, 45: 664-668, 1911-12.
- The influence of the researches of Pasteur and Lister on surgical pathology. By H. C. Cameron. *Canad. J. M. & S.*, 31: 311-322, 1912.
- Lister's work and teaching. By Sir W. W. Cheyne. *Clin. J. Lond.*, 41: 257-266, 1912-13. Also: *Tr. M. Soc., Lond.*, 36: 1-19, 1912-13.
- Lister, an appreciation. By J. B. Huber. *Am. Pract., N. Y.*, 46: 116-122, 1912.
- Persönliche Erinnerungen an Joseph Lister. By Madelung. *Strassb. med. Zeitg.*, 9: 55-60, 1912.
- Lister in Glasgow. By A. E. Malloch. *Canada Lancet*, 45: 656-658, 1911-12.
- Some memories of Mr. Lister. By A. E. Malloch. *Canad. J. M. & S.*, 31: 331-336, 1912.
- Personal reminiscences of Lister. By A. E. Malloch. *Canad. M. Ass. J.*, 2: 502-506, 1912.
- Joseph Lister in seiner Bedeutung für das Rettungswesen. By O. Marcus. *Zeitschr. f. Samariter-u. Rettungsw.*, Leipz., 18: 41, 1912.
- Personal reminiscences of Lord Lister. By H. A. Marcy. *Canada Lancet*, 45: 669-671, 1911-12.
- Personal reminiscences of Lord Lister; the introduction and development of antiseptic surgery in America. By H. A. Marcy. *Am. J. Surg.*, 26: 97-101, 1912.
- Reminiscences of the late Lord Lister. By R. H. Marten & W. T. Hayward. *Australas. M. Gaz.*, 31: 293-297, 1912.
- The funeral of Lord Lister. By Sir W. Osler. *Canad. M. Ass. J.*, 2: 343, 1912.

- A reminiscence of Lister. By L. S. Pilcher. Long Island M. J., pp. 122-124, 1912.
- Lister and his relation to the discovery of the antiseptic principle of the treatment of wounds. By B. Foster. St. Paul M. J., 14: 601-610, 1912.
- Personal recollections of Lord Lister. By F. LeM. Grasett. Canad. J. M. & S., 31: 296-310, 1912.
- Lister in Edinburgh. By F. LeM. Grasett. Canada Lancet, 45: 658-661, 1911-12.
- Personal recollections of Lord Lister. By F. LeM. Grasett. Dominion M. Month., 38: 181-194, 1912.
- Lister, man of science, surgeon, teacher. By D. B. Hart. Univ. M. Rec. Lond., 1: 193-201, 1912.
- Lord Lister; his life and work. By G. T. Wrench. 383 pp., 8°, London, T. F. Unwin, 1913.
- Biography. By E. Burci. Atti d. Accad. med. fis. fiorent., 1912, Firenze. pp. 19-24, 1913.
- Biography. By W. W. C. Proc. Roy. Soc. Lond., 86: s.B., pp. i-xxi, 1913.
- Biography. By F. H. Gerrish. Tr. Am. Surg. Ass., 21: pp. xxxi-xxxiv, 1913.
- Lister. By S. Paget. Cornhill Mag., 35: 604-611, 1913.
- Lister, the laboratory and the bedside. By R. H. Russell. Austral. M. J., 3: 1437-1444, 1913-14. Also: Brit. M. J., 1: 745-748, 1914. Also: N. Zealand M. J., 13: 115-131, 1914.
- Lister and antiseptic surgery. By Sir R. J. Godlee. Surg. Clin., Chicago, 3: 91-95, 1914.
- Tribute to Lister. By Lucas-Championnière. Tr. Internat. Cong. Med., 1913, Lond., 1914, Sect. 7, Surg., p. 2, 5.
- Lord Lister. By Sir W. Macewen. Proc. Roy. Inst. Gr. Brit., 1911-13, Lond., 20: pt. 2, 546-564, 1914.
- An address on "Lord Lister." By Sir H. Allen. Med. J. Australia, 1: 25-27, 1914.
- Personal reminiscences of Lister. By H. A. Marcy. Med. Pickwick, Saranac Lake, p. 235-237, 1915.
- Biography. By T. L. Cramhall. Univ. Durham Coll. Med. Gaz., 17: 45; 62, 1916-17.

- Lord Lister. By Sir R. J. Godlee. 8°, London, 1917. 2 ed., 1918. 3 ed., 1924.
- Biography. Hospital, Lond., 63: 351; 371; 393; 415, 1917-18.
- Lister on the use of animals in research. By W. M. Keen. J. Am. M. Ass., 68: 53, 1917.
- What Lister did. By J. Haddon. Med. Press, Lond., n.s. 105: 227, 1918.
- An appreciation of Sir John Rickman Godlee's life of Lord Lister. By J. Stewart. Canad. M. Ass. J., 8: 753-757, 1918.
- A house-surgeon's memories of Joseph Lister. By Sir St. C. Thomson. Ann. Med. Hist., 2: 93-108, 1919. Also: Mod. Hosp., 13: 1, 1919.
- Unveiling of Lister memorial tablets. Nature, London, 104: 322, 1919.
- Biography. By F. R. Packard. Ann. Med. Hist., 2: 208, 1919.
- The coming of Lister to London. By Sir St. C. Thomson. St. Barth. Hosp. J., 28: 54; 67, 1920-21.
- Lister, his life and work. By P. F. Clark. Scient. Monthly, 11: 518-539, 1920.
- Reminiscences of Lister and war work. By A. Corless. Canad. Pract. & Rev., 45: 411, 1920; 46: 1, 1921.
- Presentation of memento of Lord Lister for the custodianship case. By R. Abbe. Tr. Coll. Phys., Phila., 3.s., 43: 146-148, 1921.
- Lord Lister, the discoverer of the antiseptic system of surgery. By E. Cohen. Discovery, Lond., 2: 22-24, 1921.
- Biography. By H. L. Staples. Journal-Lancet, 42: 439-444, Sept. 1, 1922.
- Lord Lister and his priceless gift to man. By J. A. Hunnicutt, Jr., J. M. A. Georgia, 11: 473-475, 1922.
- Lord Lister. By Cuthbert Dukes. 12°, Lond., L. Parsons; Boston, Small, Maynard & Co., 1924.
- Biography. By J. H. Barclay. Univ. Durham Coll. Med. Gaz., 25: 25-35, 1924-25.
- Centenary of founders of modern scientific medicine and surgery, Pasteur and Lister. By H. G. Wetherill. Colorado Med., 21: 29-33, 1924.
- Biography. M. J. & Record, 120: 444-447, 1924.

- Biography. By H. C. Cameron. Glasgow M. J., 102: 209-214, 1924.
- Surgical reminiscence of Lister. By J. Patrick. Ibid., 101: 148-150, 1924.
- Glasgow memorial to Lord Lister. Lancet, 2: 625, 1924.
- Lister and his achievement; being the first Lister memorial lecture delivered at the Royal College of Surgeons of England on May 14, 1925 by Sir William Watson Cheyne. Lancet, 1: 1011-1018, 1925. Also: Brit. M. J., 1: 923-926, 1925. Also: 8°, London & N. Y., Longmans, Green & Co., 1925.
- The place of Lord Lister in the field of surgery. By G. W. Middleton. Am. Med., n.s. 20: 544-552, 1925.
- Lister and the ligature; a landmark in the history of modern surgery. New Brunswick, N. Y., Johnson & Johnson, 1925.
- Personal recollections. By W. W. Keen. Surg., Gynec. & Obst., 45: 861-864, 1927.
- Presentation of Lister memorial tablet. By H. G. Wetherill. Ibid., 45: 858-860, 1927.
- Presentation of replicas of Lister exhibition. By H. S. Wellcome. Ibid., 45: 856-858, 1927.
- Recent books about Lister; centenary contribution. By R. S. Skirving. M. J. Australia, 2: 87-90, 1927.
- Recollections of Lister by J. P. zum Busch. Deutsche med. Wochenschr., 53: 583-585, 1927.
- Lister letter and case report: case of ascites due to cirrhosis of liver cured by operation. By R. Morison & D. Drummond. Newcastle M. J., 7: 247, 1927.
- Lister or Bottini? By A. Clerici. Illust. med. ital., 9: 961, 1927.
- Listeriana. Irish J. M. Sc., pp. 557-560, 1927.
- Listerism in Germany. By M. von Gruber. München. med. Wochenschr., 74: 592, 1927.
- Lord Lister and the renaissance of surgery. By E. L. Gilcrest. S. Clin. North America, 7: 1117-1123, 1927.
- Lord Lister's life and work. By A. Young. Janus, 31: 318-335, 1927.

- Historical sketch. By C. F. Painter. Boston M. & S. J., 196: 1093-1096, 1927.
- Lister's influence on modern surgery. By G. M. Ohmart. J. Michigan M. Soc., 26: 679-681, 1927.
- Letter of Lord Lister. Deutsche med. Wochenschr., 53: 585, 1927.
- Lister and malaria. Science Prog., 22: 114-116, 1927.
- Lister and West London Medico-Chirurgical Society. By F. J. McCann. West London M. J., 32: 148-152, 1927.
- Lister and physiology. By C. S. Sherrington. Nature, London, 119: 606-608, 1927.
- Lister celebrations in London. Ibid., 119: 570-572, 1927.
- Methods in surgery. By W. W. Cheyne. Ibid., 120: 161, 1927.
- Lister's contribution to preventive medicine. By C. J. Martin. Ibid., 119: 529-531, 1927.
- Lister's scientific work. By W. Bullock. Ibid., 119: 531-533, 1927.
- What Lord Lister's work has meant to surgery. By R. J. Reed. W. Virginia M. J., 23: 330-332, 1927.
- Centenary of Lister; tale of sepsis and antisepsis. By A. P. C. Ashhurst. Ann. M. Hist., 9: 205-221, 1927.
- Comparative contributions of Lister and Osler. By W. B. Munro. California & West. Med., 27: 44-47, 1927.
- (Lister). Emancipators. By H. Cushing. Lancet, 2: 185-186, 1927. Also: Boston M. & S. J., 197: 651-652, 1927.
- Biography. By C. Kaufmann. Schweiz. med. Wochenschr., 57: 313-315, 1927.
- Biography. By V. Schaldemose. Ugesk. f. Laeger, 89: 267-273, 1927.
- Biography. By V. Schmieden. Klin. Wochenschr., 6: 721, 1927.
- Biography. By J. A. Spalding. J. Maine M. A., 18: 149-153, 1927.
- Biography. By G. Turner. Vrach. Gaz., 31: 643-646, 1927.
- Biography. By A. Vedrani. Illust. med. ital., 9: 87-96, 1927.
- Address on approach to surgery. By B. Moynihan. Brit. M. J., 2: 621-624, 1927.

- Appreciation of Lord Lister. By J. Bland-Sutton. Surg., Gynec. & Obst., 45: 867-868, 1927.
- Lister as physiologist. By J. Tait. Science, 66: 267-272, 1927.
- Biography. Presse méd., 35: 523, 1927.
- Biography. By W. Boyd. Journal-Lancet, 47: 557-564, 1927.
- Biography. By D. Cheever. Boston M. & S. J., 196: 984-993, 1927.
- Biography. By A. Eiselberg. Wien. klin. Wochenschr., 40: 461-465, 1927.
- Biography. By J. L. Gibson. M. J. Australia, 1: 844-850, 1927.
- Biography. By C. E. Goddard. Ibid., 1: 850-856, 1927.
- Biography. By H. von Haberer. Deutsche med. Wochenschr., 53: 582, 1927.
- Biography. By H. L. Harley. J. M. Soc. New Jersey, 24: 557-561, 1927.
- Biography. By N. B. Harman. West London M. J., 32: 57-60, 1927.
- Biography. By H. Hartmann. Bull. Acad. de méd., Paris, 97: 469-473, 1927. Also: Gaz. d. hôp., 100: 509, 1927.
- Biography. By L. L. Hill. Am. J. Surg., 3: 99-110, 1927.
- Lister centenary celebrations in London. M. J. & Rec., 125: 706, 768, 1927.
- Lister; house-surgeon's memories. By S. Thomson. Brit. M. J., 1: 659-662, 1927. Also: Lancet, 1: 775-780, 1927. Abridged in: M. J. & Rec., 125: 772-773, 1927.
- Lord Lister as pathologist and bacteriologist. By W. Bullock. Brit. M. J., 1: 654-656, 1927. Also: Lancet, 1: 744-746, 1927.
- Recollections of Lister. By C. E. Wallis. J. Am. Dent. A., 14: 707-713, 1927.
- Hunter's ideal and Lister's practice. By B. Moynihan. Brit. M. J. 1: 313-319, 1927. Abridged in: Lancet, 1: 373-379, 1927.
- Lister as a physiologist. By C. S. Sherrington. Brit. M. J., 1: 653-654, 1927. Also: Lancet, 1: 743-744, 1927.
- Lister as a surgeon. By B. Moynihan. Brit. M. J., 1: 656-658, 1927. Also: Lancet, 1: 746-748, 1927.

- Lister centenary. By E. Chapman. *Hygeia*, 5: 193, 1927.
- Lister centenary celebrations. Glasgow M. J., 107: 265-189, 1927.
- The conquest of sepsis. By Sir J. Bland-Sutton. *Lancet*, 1: 781-786, 1927.
- Biography. By N. B. Harman. *Canad. M. A. J.*, 17: 589-590, 1927.
- Biography. By E. St. Jacques. *Ibid.*, 658-661, 1927.
- Case of excision of knee and elbow joints by Lord Lister; condition 40 years later. By G. T. Beatson. *Brit. M. J.*, 1: 662-663, 1927.
- Domestic survey. By H. Rolleston. *Lancet*, 1: 780-781, 1927.
- Remembrances of Lord Lister. By R. Morison. *Newcastle M. J.*, 7: 242-246, 1927.
- Reminiscences of 50 years ago. By F. R. Cross. *Bristol Med.-Chir. J.*, 44: 112A-112D, 1927.
- Lister and modern surgery. By H. W. Orr. *Nebraska M. J.*, 12: 411-416, 1927.
- Surgical instruments designed by Lister. By C. J. S. Thompson. *Boston M. & S. J.*, 196: 946-951, 1927.
- Centenary; tale of sepsis and antisepsis. By A. P. C. Ashhurst. *Tr. Coll. Physicians*, 49: 70-93, 1927.
- The man and his achievements. By E. L. Gilcrest. *Tr. South. S. A.*, 40: 166-174, 1927.
- Lister centenary volume. Edited by J. L. Turner. *Edinburgh, Oliver & Boyd*, 1927.
- Lister as I knew him. By J. R. Leeson. *N. Y., Wood*, 1927.
- My reminiscences of Lord Lister in Edinburgh. By F. L. Grasett. *Pub. Health J.*, 19: 115-118, 1928.
- Personal recollections. By W. W. Keen. *Hygiea*, 90: 66-75, 1928.
- Personal reminiscences. By E. St. G. Baldwin. *Pub. Health J.*, 19: 112-114, 1928.
- Biography. By F. K. Boland. *South. M. J.*, 21: 33-35, 1928.
- Anecdote of Lord Lister. By J. Riddell. *M. J. & Rec.*, 126: 747, 1927.
- Lister as scientist. By J. J. R. Macleod. *Pub. Health J.*, 19: 101-111, 1928.

- Lister as scientist. By G. E. Seaman. *Wisconsin M. J.*, 27: 51; 99, 1928.
- Lister's influence on modern surgery. By H. C. Mack. *J. Michigan M. Soc.*, 27: 33-41, 1928.
- Life of Lister. By E. J. Horgan. *Virginia M. Monthly*, 54: 607-612, 1928.
- A paper that inaugurated a new surgical era. (New method of treating compound fracture, abscess, etc.) By T. S. W. *Am. J. Surg.*, 7: 287-289, 1929.
- Letters. (Briefe aus vergangenen Tagen.) *Deutsche med. Wochenschr.*, 56: 24, 1930.
- Semmelweis and Lister. By B. A. G. Veraart. *Nederl. tijdschr. v. geneesk.*, 74: 1762-1775, 1930.
- Biography. By E. P. Quain. *Minnesota Med.*, 13: 445-450, 1930.
- Lister—the idealist; Listerian oration. By Moynihan. *Brit. M. J. (Canad. suppl.)* pp. 7-12, 1930, Also: *Canad. M. A. J.*, 23: 479-488, 1930.
- Biography. By J. Alvarez Sierra. *Día méd.*, 3: 521, 1931.
- Lister's early bacteriological researches and origin of his antiseptic system; Listerian oration. By C. Martin. *M. J. Australia*, 2: 437-444, 1931.
- Lister; pioneer of medicine. By C. Lillingston. *Hygeia*, 10: 144-147, 1932.
- House-surgeon's memories of Lister. By St. C. Thomson. *Birmingham M. Rev.*, 7: 300-311, 1932.
- A student under Lister; Anne Mackenzie oration. By R. H. Russell. *M. J. Australia*, 1: 669-674, 1932.
- Eight letters of Lister to William Sharpey. By C. R. Rudolf. *Brit. J. Surg.*, 20: 145-164, 1932; 20: 459-466, 1933.
- Agostino Bassi, early parasitologist (work of Bassi, Lister and Semmelweis and review of development of conception of contagion). By L. Münster. *Janus*, 37: 221-246, 1933.
- Lister and his time. By C. Ballance. *Lancet*, 1: 815-816, 1933.
- Lister and wiring patella; ipsissima verba. By D'A. Power. *Brit. J. Surg.*, 21: 557-559, 1934.

- Lister's rôle in progress of surgery. By R. Muñoz Carbonero.
Crón. méd., Valencia, 38: 158-160, 1934.
- Lister as physiologist; Listerian oration. By W. A. Osborne.
M. J. Australia, 1: 761-765, 1935.
- Life, work and character; Listerian oration. By H. Newland.
M. J. Australia, 1: 263-270, 1935.
- Great physician, who founded the science of modern surgery.
By A. Berlin. Hygeia, 13: 643, 1935.
- Lister's mind and character. By E. Archibald. Canad. M.
A. J., 35: 475-490, 1936.



On a New Method of Treating Compound Fracture, Abscess, Etc., with Observations on the Conditions of Suppuration

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PART I. ON COMPOUND FRACTURE

THE frequency of disastrous consequences in compound fracture, contrasted with the complete immunity from danger to life or limb in simple fracture, is one of the most striking as well as melancholy facts in surgical practice.

If we inquire how it is that an external wound communicating with the seat of fracture leads to such grave results, we cannot but conclude that it is by inducing, through access of the atmosphere, decomposition of the blood which is effused in greater or less amount around the fragments and among the interstices of the tissues, and, losing by putrefaction its natural bland character, and assuming the properties of an acrid irritant, occasions both local and general disturbance.

We know that blood kept exposed to the air at the temperature of the body, in a vessel of glass or other material chemically inert, soon decomposes; and there is no reason to suppose that

the living tissues surrounding a mass of extravasated blood could preserve it from being affected in a similar manner by the atmosphere. On the contrary, it may be ascertained as a matter of observation that, in a compound fracture, twenty-four hours after the accident the coloured serum which oozes from the wound is already distinctly tainted with the odour of decomposition, and during the next two or three days, before suppuration has set in, the smell of the effused fluids becomes more and more offensive.

This state of things is enough to account for all the bad consequences of the injury.

The pernicious influence of decomposing animal matter upon the tissues has probably been underrated, in consequences of the healthy state in which granulating sores remain in spite of a very offensive condition of their discharges. To argue from this, however, that fetid material would be innocuous in a recent wound would be to make a great mistake. The granulations being composed of an imperfect form of tissue, insensible and indisposed (p. 327) to absorption, but with remarkably active cell-development, and perpetually renovated as fast as it is destroyed at the surface, form a most admirable protective layer, or living plaster. But before a raw surface has granulated, an acrid discharge acts with unrestrained effect upon it, exciting the sensory nerves, and causing through them both local inflammation and general fever, and also producing by its caustic action a greater or less extent of sloughs, which must be thrown off by a corresponding suppuration, while there is at the same time a risk of absorption of the poisonous fluids into the circulation.

This view of the cause of the mischief in compound fracture is strikingly corroborated by cases in which the external wound is very small. Here, if the coagulum at the orifice is allowed to dry and form a crust, as was advised by John Hunter,* all bad consequences are probably averted, and, the air being excluded, the blood beneath becomes organised and absorbed, exactly as

* See *Works of J. Hunter*, edited by Palmer, vol. i., p. 429.

in a simple fracture. But if any accidental circumstance interferes with the satisfactory formation of the scab, the smallness of the wound, instead of being an advantage, is apt to prove injurious, because, while decomposition is permitted, the due escape of foul discharges is prevented. Indeed, so impressed are some surgeons with the evil which may result from this latter cause, that, deviating from the excellent Hunterian practice, they enlarge the orifice with the knife in the first instance and apply fomentations, in order to mitigate the suppuration which they render inevitable.

Turning now to the question how the atmosphere produces decomposition of organic substances, we find that a flood of light has been thrown upon this most important subject by the philosophic researches of M. Pasteur, who has demonstrated by thoroughly convincing evidence that it is not to its oxygen or to any of its gaseous constituents that the air owes this property, but to minute particles suspended in it, which are the germs of various low forms of life, long since revealed by the microscope, and regarded as merely accidental concomitants of putrescence, but now shown by Pasteur to be its essential cause, resolving the complex organic compounds into substances of simpler chemical constitution, just as the yeast-plant converts sugar into alcohol and carbonic acid.

A beautiful illustration of this doctrine seems to me to be presented in surgery by pneumothorax with emphysema, resulting from puncture of the lung by a fractured rib. Here, though atmospheric air is perpetually introduced into the pleura in great abundance, no inflammatory disturbance supervenes; whereas an external wound penetrating the chest, if it remains open, infallibly causes dangerous suppurative pleurisy. In the latter case the blood and serum poured out into the pleural cavity, as an immediate consequence of the injury, are decomposed by the germs that enter with the air, and then operate as a powerful irritant upon the serous membrane. But in case of puncture of the lung without external wound, the atmospheric gases are filtered of the causes of decomposition before they enter the pleura, by passing through the bronchial tubes, which, by their small size, their tortuous course, their mucous secretion, and cili-

ated epithelial lining, seem to be specially designed to arrest all solid particles in the air inhaled. Consequently the effused fluids retain their original characters unimpaired, and are speedily absorbed by the unirritated pleura.

Applying these principles to the treatment of compound fracture, bearing in mind that it is from the vitality of the atmospheric particles that all the mischief arises, it appears that all that is requisite is to dress the wound with some material capable of killing these septic germs, provided that any substance can be found reliable for this purpose, yet not too potent as a caustic.

In the course of the year 1864 I was much struck with an account of the remarkable effects produced by carbolic acid upon the sewage of the town of Carlisle, the admixture of a very small proportion not only preventing all odour from the lands irrigated with the refuse material, but, as it was stated, destroying the entozoa which usually infest cattle fed upon such pastures.

My attention having for several years been much directed to the subject of suppuration, more especially in its relation to decomposition, I saw that such a powerful antiseptic was peculiarly adapted for experiments with a view to elucidating that subject, and while I was engaged in the investigation the applicability of carbolic acid for the treatment of compound fracture naturally occurred to me.

My first attempt of this kind was made in the Glasgow Royal Infirmary in March, 1865, in the case of compound fracture of the leg. It proved unsuccessful, in consequence, as I now believe, of improper management; but subsequent trials have more than realised my most sanguine anticipations.

Carbolic acid* proved in various ways well adapted for the

* Carbolic acid is found in the shops in two forms—the glacial or crystalline, solid at ordinary temperatures of the atmosphere; and the fluid, which sometimes passes under the name of German creasote. The fluid variety is sold in various degrees of purity. The crude forms are objectionable from their offensive odour; but the properly rectified product is almost fragrant. Different samples, however, differ much in energy of action, and hence, though I have hitherto employed the liquid kind in compound fracture, it would probably be better to use the crystallised form, melting it by placing the vessel containing it in warm water for a few minutes. Carbolic acid is almost absolutely insoluble in water, but dissolves readily in various organic liquids, such as the common fixed oils or glycerine.

purpose. It exercises a local sedative influence upon the sensory nerves; and hence is not only almost painless in its immediate action on a raw surface, but speedily renders a wound previously painful entirely free from uneasiness. When employed in compound fracture its caustic properties are mitigated so as to be unobjectionable by admixture with the blood, with which it forms a tenacious mass that hardens into a dense crust, which long retains its antiseptic virtue, and has also other advantages, as will appear from the following cases, which I will relate in the order of their occurrence, premising that, as the treatment has been gradually improved, the earlier ones are not to be taken as patterns.

CASE 1.—James G—, aged eleven years, was admitted into the Glasgow Royal Infirmary on August 12th, 1865, with compound fracture of the left leg, caused by the wheel of an empty cart passing over the limb a little below its middle. The wound, which was about an inch and a half long, and three-quarters of an inch broad, was close to, but not exactly over, the line of fracture of the tibia. A probe, however, could be passed beneath the integument over the seat of fracture and for some inches beyond it. Very little blood had been extravasated into the tissues.

My house-surgeon, Dr. Macfee, acting under my instructions, laid a piece of lint dipped in liquid carbolic acid upon the wound, and applied lateral pasteboard splints padded with cotton wool, the limb resting on its outer side, with the knee bent. It was left undisturbed for four days, when, the boy complaining of some uneasiness, I removed the inner splint and examined the wound. It showed no signs of suppuration, but the skin in its immediate vicinity had a slight blush of redness. I now dressed the sore with lint soaked with water having a small proportion of carbolic acid diffused through it; and this was continued for five days, during which the uneasiness and the redness of the skin disappeared, the sore meanwhile furnishing no pus, although some superficial sloughs caused by the acid were separating. But the epidermis being excoriated by this dressing, I substituted for it a solution of one part of carbolic acid in from ten to twenty

parts of olive oil, which was used for four days, during which a small amount of imperfect pus was produced from the surface of the sore, but not a drop appeared from beneath the skin. It was now clear that there was no longer any danger of deep-seated suppuration, and simple water-dressing was employed. Cicatrisation proceeded just as in an ordinary granulating sore. At the expiration of six weeks I examined the condition of the bones, and, finding them firmly united, discarded the splints; and two days later the sore was entirely healed, so that the cure could not be said to have been at all retarded by the circumstance of the fracture being compound.

This, no doubt, was a favourable case, and might have done well under ordinary treatment. But the remarkable retardation of suppuration, and the immediate conversion of the compound fracture into a simple fracture with a superficial sore, were most encouraging facts.

CASE 2.—Patrick F——, a healthy labourer, aged thirty-two, had his right tibia broken on the afternoon of Sept. 11th, 1865, by a horse kicking him with its full force over the anterior edge of the bone about its middle. He was at once taken to the infirmary, where Mr. Miller, the house-surgeon in charge, found a wound measuring about an inch by a quarter of an inch, from which blood was welling profusely.

He put the fracture in pasteboard splints, leaving the wound exposed before their anterior edges, and dressing it with a piece of lint dipped in carbolic acid, large enough to overlap the sound skin about a quarter of an inch in every direction. In the evening he changed the lint for another piece, also dipped in carbolic acid, and covered this with oiled paper.* I saw the patient the next day, and advised the daily application of a bit of lint soaked in carbolic acid over the oiled paper; and this (p. 328) was done for the next five days. On the second day there was an oozing of red fluid from beneath the dressing, but by the third day this had ceased entirely. On the fourth day, when, under ordinary circumstances, suppuration would have

* A cheap substitute for oiled silk, devised by the late Dr. M'Ghee, of the Glasgow Infirmary, and very useful for covering poultices, &c.

made its appearance, the skin had a nearly natural aspect, and there was no increase of swelling, while the uneasiness he had previously felt was almost entirely absent. His pulse was 64, and his appetite improving. On the seventh day, though his general condition was all that could be wished, he complained again of some uneasiness, and the skin about the still adherent crust of blood, carbolic acid and lint, was found to be vesicated, apparently in consequence of the irritation of the carbolic acid. From the seventh day the crust was left untouched till the eleventh day, when I removed it, disclosing a concave surface destitute of granulations, and free from suppuration. Water-dressing was now applied, and by the sixteenth day the entire sore, with the exception of one small spot where the bone was bare, presented a healthy granulating aspect, the formation of pus being limited to the surface of the granulations.

I now had occasion to leave Glasgow for some weeks, and did so feeling that the cure was assured. On my return, however, I was deeply mortified to learn that hospital gangrene attacked the sore soon after I went away, and made such havoc that amputation became necessary.

While I could not but feel that this case, by its unfortunate issue, might lose much of its value in the minds of others, yet to myself it was perfectly conclusive of the efficacy of carbolic acid for the object in view. At the same time it suggested some improvement in matters of detail. It showed that the acid may give rise to a serous exudation apt to irritate by its accumulation, and therefore that a warm and moist application would be advantageous to soothe the part, and also ensure the free exit of such exuded fluid. At the same time it appeared desirable to protect the crust with something that would retain the volatile organic acid more effectually than oiled silk or gutta percha, through which it makes its way with the utmost facility. For this purpose a metallic covering naturally suggested itself, and as ordinary tin-foil is unsuitable from its porosity, I employed thin sheet-lead, and afterwards block tin, such as is used for covering the jars of anatomical preparations, superior to lead on account of the facility with which it can be moulded to any shape that is desired.

For a long time, however, I had no opportunity of giving this improvement a trial, the compound fractures admitted into my wards during the next eight months being merely two cases with small wounds. One of these was a fracture of the ulna into the elbow-joint in a woman so old that suppuration, had it occurred, would probably have proved fatal. The orifice in the integument was extremely small, and all would most likely have gone on well had the bit of dry lint applied to check the free bleeding from the interior been left undisturbed, instead of being saturated with carbolic acid as it was. This, however, could not but be an additional safeguard, and at the same time it was satisfactory to find that the caustic application did not interfere with the usual healing by scabbing, cicatrisation being found complete when the crust was removed.

The other case was a fracture of the humerus a little above the elbow in a young man, caused by a fall from a height of thirty-five feet, the wound, which was not quite half an inch in length, being situated at the inner side of the limb, where it must necessarily be covered by a splint. Dr. Watson, then my house-surgeon, applied lint dipped in carbolic acid covered with a slightly concave piece of sheet-lead about as large as a shilling, and put up the limb in pasteboard padded with cotton. At the end of ten days the inner side of the limb was uncovered for the first time, and merely as a matter of curiosity, when the lead, with the lint adhering to it, dropped off, disclosing a small superficial granulating sore without the slightest suppuration, just as in ordinary healing by scabbing. This case is interesting, not so much because the compound fracture was converted into a simple one, for this might have occurred under ordinary treatment, but because it showed that in any case of fracture complicated with a small wound, we have in carbolic acid a means which enables us to disregard the wound altogether after the splints have been applied, instead of being under the necessity of daily disturbing the apparatus to change the dressing.

At length a case presented itself well calculated to test the value of carbolic acid in compound fracture.

CASE 3.—John H—, aged twenty-one, a moulder in an iron foundry, was admitted on May 19th, 1866, with compound fracture of the left leg, produced in the following manner. He was superintending the raising by crane of an iron box containing sand ready for a casting, the box and its contents weighing about 12 cwt., when one of the chains by which it was suspended slipped, and the box fell from the height of four feet with unbroken force upon the inner side of his leg, which was planted obliquely beneath it. Both bones were fractured, the tibia about its middle, and a wound an inch and a half in length, and three-quarters of an inch broad, was made at the inner aspect of the limb, on a level with the fracture of the tibia, and obviously communicating with it. At the same time the soft parts generally were much confused, as was evident from the great distension of the limb with extravasated blood. Dr. A. Cameron, my house-surgeon, finding, on manipulating the limb, that bubbles escaped along with the blood, implying that air had been introduced during the movements of the leg as the patient was being carried to the infirmary, thought it best that I should see the case, which I did at three P.M., three hours and a half after the accident. In order to expel the air I squeezed out as much as I could of the clotted and fluid blood which lay accumulated beneath the skin, and then applied a bit of lint dipped in carbolic acid slightly larger than the wound, and over this a piece of sheet tin about four inches square. Finally the limb was placed in pasteboard splints, resting on its outer side with the knee bent. At eight P.M. some more acid was added with another piece of lint, so that the crust of clots, carbolic acid and lint, was about one-third of an inch in thickness. A hot fomentation also was applied over the inner aspect of the leg, the crust being protected by the tin. Next day he was pretty easy, and had passed a quiet night, though occasionally awakened by starting pains; the pulse was 90, but he took some food with relish. The surface of the crust was touched again with carbolic acid, and the fomentation was continued, and in place of the internal pasteboard splint, a large sheet of tin was applied over the flannel from the knee to the ankle, being retained in position

by looped bandages. This proved a very satisfactory arrangement, the tin having sufficient firmness to answer the purpose of a splint, which, again, served as an excellent padding. The fomentation was changed night and morning, and gave great comfort to the patient, and once a day carbolic acid was applied lightly to the crust.

Two days after the accident the limb was easier, but the circumferential measurement of the calf continued the same, and the pulse was 96, though soft. On the fourth day—the critical period with reference to suppuration—the limb was free from pain, and the calf less tense, and distinctly reduced in dimensions; while the pulse had fallen to 80, and the patient had enjoyed his food after a good night's rest. After this the swelling steadily subsided, the skin remaining, as it had been from the first, free from the slightest inflammatory blush, and his general health was in all respects satisfactory. Seven days after the receipt of the injury there was some puriform discharge from the surface of the skin where the carbolic acid, confined by the smaller piece of tin that covered the crust, had produced excoriation by its caustic action; and to prevent needless irritation from this cause, the tin was reduced so as to leave only a narrow flat rim round a bulging part which corresponded to the crust.

About a fortnight after the accident a sense of fluctuation was experienced over the seat of fracture, but, as all was going on favourably otherwise, I hoped that this was due simply to serum from the effused blood; and in a few days it had completely disappeared, not a drop of pus meanwhile having escaped from beneath the crust. About this time the edges of the crust became softened by the superficial discharge from the surrounding parts, and these softened portions were daily clipped away with scissors. Thus the circumferential part of the crust which had overlapped the skin was removed, and that which lay over the extravasated blood in the wound was also reduced to smaller and smaller size.

On the 7th of June, nearly three weeks after the accident, an observation of much interest was made. I was detaching a portion of the adherent crust from the surface of the vascular

structure into which the extravasated blood beneath had been converted by the process of organisation, when I exposed a little spherical cavity about as big as a pea, containing brown serum, forming a sort of pocket in the living tissues, which when scraped with the edge of a knife, bled even at the very margin of the cavity. This appearance showed that the deeper portions of the crust itself had been converted into living tissue. For cavities formed during the process of aggregation, like those with clear liquid contents in a Gruyère cheese, occur in the grumous mass which results from the action of carbolic (p. 329) acid upon blood; and that which I had exposed had evidently been one of these, though its walls were now alive and vascular. Thus the blood which had been acted upon by carbolic acid, though greatly altered in physical characters, and doubtless chemically also, had not been rendered unsuitable for serving as pabulum for the growing elements of new tissue in its vicinity. The knowledge of this fact is of importance; as it shows that, should circumstances appear to demand it, we may introduce carbolic acid deeply among the blood extravasated in a limb, confident that all will nevertheless be removed by absorption. A few days later all traces of the little cavity had become obliterated by the granulating process.

At the close of the third week the application of carbolic acid to the crust was discontinued, and the original internal paste-board splint padded with cotton was again employed, instead of the tin and fomentation. What remained of the crust was still kept protected with the tin cap, with the view of ascertaining how long it would continue to adhere; and at length, nearly four weeks after the accident, I tore it off from the vascular surface beneath, which bled as I did so. The crust had preserved the subjacent parts from disturbance as effectually as if it had been a piece of living integument; and it is worthy of remark that the vascular surface below had not the pulpy softness of granulations, but was comparatively firm and substantial. The bit of crust still smelt of carbolic acid, though none had been applied for five days.

At the expiration of six weeks from the receipt of the injury

the fragments were found firmly united in good position, just as if the fracture had been a simple one, though the cicatrisation of the rather extensive sore was not complete till a later period.

CASE 4.—James W——, aged ten, was engaged in a turner's factory worked by steam power on the 8th of June, 1866, when his right arm was drawn in between a strap and a shaft turned by it. He called out for assistance, but thinks two minutes must have elapsed before the machinery was stopped, and during the whole of this time the strap, which was still moving while he held the arm steady, was cutting into the ulnar side of the forearm, breaking through the ulna about its middle, while the radius was bent with "green-stick" fracture. He was taken at once to the infirmary, where the wound was found to be about an inch and a half in depth, occupying more than half the circumference of the limb, chiefly at the dorsal aspect, but extending round also to the palmar side. The upper fragment of the ulna was protruding about an inch, and two strips of muscle, about a quarter of an inch in thickness and from two to three inches in length were hanging out; the lacerated state of the parts confirming the boy's account of the accident.

On seeing him about two hours afterwards, I sawed off the protruding portion of the ulna, and the tags of muscle having been previously clipped away, I applied carbolic acid freely to the whole interior of the wound, including the exposed surface of the bone; and having straightened the radius, which gave way during the process, placed the limb upon a wooden palmar splint. Avoiding any attempt to approximate the lips of wound, I covered it with a piece of sheet-tin, sufficiently large to overlap the sound skin about a quarter of an inch in every direction. The limb was fixed to the splint by a bandage, so arranged as to permit the removal of the tin without disturbing the apparatus; and hot fomentations were applied over the whole. A few minutes after the carbolic acid was applied he said he was perfectly easy. At seven o'clock he asked for food, and took it. His pulse was then 84. At eight P.M. I saw him again, and applied beneath the tin a piece of lint dipped in carbolic acid, about as large as the wound. Noticing some distortion in the

upper arm, I found that the humerus also was broken in its lower third, an applied splints accordingly, the limb being kept supported upon a pillow beside him. He slept a good deal during the night, though moaning and starting occasionally. Next day his pulse was 108; but he took his breakfast heartily, and the tongue was healthy, while he complained only of a little uneasiness about the elbow, and even this disappeared on changing the fomentation cloth. A piece of sheet-tin was now arranged so as to form a sort of cover for the forearm, including the hand. Being retained in position by looped bandages, it increased the steadiness of the limb, while it ensured efficiency of the fomentation.

Two days after the accident the oozing of blood and serum, which had been considerable during the previous twenty-four hours, had nearly ceased; but he still experienced comfort from the fomentation, though any pain which he felt was connected with the simple fracture of the humerus. His pulse was 88, his tongue clean and appetite good after a sound sleep at night; and from this time onward his general health continued perfectly satisfactory. On the fourth day a small quantity of pale, grey, slimy discharge was observed from beneath the crust at one part; and thinking that this might, perhaps, have occurred for want of proper action of the carbolic acid, I applied the latter with unusual freedom to the surface of the crust. This was repeated at night; and the same energetic use of the carbolic acid, twice in the twenty-four hours, was continued on the fifth day. Yet, on the sixth day, the discharge from beneath the crust, instead of being diminished, was increased, and more puriform to the naked eye; while under the microscope, there was clear indication of new cell-formation, whereas, on the day before, nothing but fibrinous material, with granular and other debris, had been discoverable. On the seventh day the discharge was still greater in amount; yet the limb remained free from pain, and was steadily diminishing in circumference, and pressure in the neighbourhood of the crust failed to induce any increase of the discharge, which appeared to be merely superficial.

In the course of the next few days it became apparent that

this discharge, so far from being the result of insufficient action of the carbolic acid, was caused by the stimulating influence of the acid itself, applied with greater freedom over a crust much thinner than that of Case 3. Suppuration from this cause is, however, productive of no mischief, as will be better understood from the sequel. That such was the case in this instance was manifest on the fourteenth day, when the crust, which was nearly detached, was removed, disclosing an appearance for which I confess I had not been prepared. In place of the deep and ragged wound was a granulating sore, nearly on a level with the skin, and pretty uniform in surface, except at one part about its middle, where there was a depression about half an inch in depth, at the bottom of which a small portion of the outer surface of the ulna was visible, bare, but of pink colour. Not only had the compound of blood and carbolic acid which had existed in the depths of the wound been organised, but the portions of tissue killed by the violence to which they had been subjected in the accident, and also those destroyed by the caustic action of the carbolic acid, had been similarly acted on, and all had been, so to speak, fused together into a living mass, without the occurrence of any deep-seated suppuration.

By the nineteenth day the exposed part of the bone was covered, and the depression in the sore obliterated by granulation, without any exfoliation occurring; and two days short of seven weeks after the accident the sore was entirely healed.

The extensive loss both of bone and of the soft parts made osseous union of the ulna a matter of difficulty, and on the 5th of August the limb was placed in a starched apparatus, to promote complete consolidation, and he was soon after discharged from the hospital.

About six weeks later he presented himself at the infirmary, and the bandage was removed in my absence, when, the bone appearing firm, he was allowed to dispense with the apparatus, and was unfortunately not directed to show himself again. In the course of a few weeks, however, he appeared with the fragments again movable. The starched bandage was therefore reapplied, but when I last saw him, some weeks ago, bony union

had not yet occurred. A good deal of osseous formation had, however, taken place, so that the fragments now overlapped each other; and should the cure be still incomplete when he next shows himself, the case will be a fair subject for Bickersteth's method of treating ununited fracture by drilling. Meanwhile, the radius being firm, and the injured extensors of the fingers having completely regained their powers, he will, in any event, have a very useful hand.

This case indicated a greater range of applicability of the treatment by carbolic acid than I had anticipated, and encouraged me to employ it under the almost desperate circumstances of the following case.

(p. 357) CASE 5.—Charles F——, a fine, intelligent boy, seven years of age, was knocked down at eight P.M. on June 23rd, 1866, by an omnibus crowded with passengers inside and out, and one if not both wheels passed over his right leg, breaking both the bones and inflicting a frightfully extensive wound. The person who brought him to the infirmary said that he had lost a great deal of blood, and the presence of a compress in the ham, placed there by the medical man who saw him at the time of the accident, corroborated this statement. When I saw the child, after an unavoidable delay of three hours, he was greatly prostrated by shock as well as hemorrhage, so much so that amputation appeared likely to afford but a slender chance of life, although the state of the injured parts seemed at first sight to admit of no alternative. The tibia, which was broken about its middle, lay exposed in a wound occupying almost the entire length and breadth of the inner aspect of the leg, reaching from the inner condyle of the femur to within an inch and a quarter of the tip of the internal malleolus; the skin having been stripped back so as to lay bare the gastrocnemius as well as the bone. The large flap of integument was perforated about two inches from its edge opposite to the seat of fracture, and there was also an opening in the skin on the outer side of the leg, implying that the violence had acted with full effect upon the whole thickness of the limb. Yet the bone was not comminuted, and the muscles, though evidently severely contused, were not much

lacerated, while the anterior tibial artery was felt beating in the foot; and, hopeless as would have been the idea of trying to save the limb by ordinary treatment, I determined to make the attempt by the help of carbolic acid.

Chloroform having been administered, the acid of full strength was applied with great freedom, the contused mass being repeatedly squeezed, to induce the liquid to insinuate itself into all its interstices, including that between the riding fragments of the tibia. The flap of skin was then brought towards its natural position, and lint soaked in the acid was placed under the wide raw surface which still remained exposed, and over the lint a piece of sheet tin. The other openings in the integument were similarly treated; and, the riding of the fragments having been corrected by extension, the limb was laid on its outer side, with the knee bent, upon an external pasteboard splint, moulded to the leg and foot, and strengthened by a temporary wooden splint. A porous cloth was applied over the tin to absorb the blood and serum which must escape from beneath its edges; and the whole apparatus was secured with a roller. At the conclusion of the dressing the pulse was 112.

He passed a restless night, though occasionally dozing, (p. 358) and the pulse next morning was 120. The bandage having been cut away sufficiently to enable the tin to be removed, the wound was found to have gaped so that the lint no longer covered the whole of it. Pieces of the cloth, which had become soaked with the exuded blood, were placed upon the exposed part, and also over the lint so as to make the crust more substantial, and the whole was freely treated with carbolic acid. The tin was then bulged out so as to be accommodated to the thickened crust, while overlapping the neighbouring skin to a slight extent; being retained in position by a couple of turns of bandage. A hot fomentation was then placed upon the inner aspect of the limb, and the whole leg enveloped in a large sheet of block-tin secured by looped bandage.

In the evening the pulse was 136, and on the following morning, thirty-six hours after the accident, it had risen to 168, and was very weak. He lay talking to himself in a rambling manner,

unable to understand what was said to him. He was extremely restless, and had taken no food whatever since his admission. During the next night, however, he became composed, and took a little milk; and on the morning of the third day he was found to be again intelligent, while the pulse had fallen to 140, and was of fair strength. The skin in the vicinity of the injury, both at the knee and ankle, was free from discoloration or swelling; but part of the large flap of skin over the calf was of purple tint, and had evidently lost its vitality. This dead part was touched with carbolic acid, to preserve it from decomposition, and convert it into a crust for the protection of the subjacent textures, and an additional piece of tin was applied to cover it. A good deal of brown transparent fluid escaped from beneath the crust.

On the fourth day the pulse was 120; he was quite bright and tranquil, and said he felt no pain. There was still no odour about the injured part, except that of carbolic acid. The discharge was much diminished, and was principally serous.

By the sixth day the pulse was as low as 108. He had a hearty appetite, and also took with avidity the six ounces of port wine allowed him during the twenty-four hours. His tongue, which had previously been dry, was moist. He had slept well at night, though waking occasionally with a scream. The discharge from beneath the crust, trifling in amount, was chiefly serous.

On the eighth day the splint was removed for the first time, and was covered with sheet-tin in order to prevent the discharge from softening the pasteboard. The leg had become slightly bent inwards through the yielding of the splint; and when it was now straightened, the upper margin of the crust became detached, exposing a deep granulating cavity. A bit of lint, dipped in carbolic acid, was applied lightly over this opening, and the tin was readjusted so as to cover it. Pressure in the neighborhood of the injured part, about the knee, ankle, and calf, failed to induce the slightest increase of the discharge, which was thus shown to come merely from the surface beneath the crust, and was still for the most part transparent.

At the close of the second week his state was on the whole very favorable. His general health was much improved; and

although he still suffered occasionally, especially at night, from restless movements of the limb, these had been much restrained by a new splint, extending from half way up the thigh to the toes. The wound was certainly very large, measuring eight inches in length by six in greatest width; but it was healing round almost the entire circumference. In order to permit cicatrification, which carbolic acid tends to check, the detached edges of the crust had been clipped away, and the exposed narrow ring of granulations was dressed with lint dipped in a solution of sulphite of potash—five grains to an ounce of water. The crust, however, was still touched daily as before with carbolic acid, while the tin still covered the whole of the injured part. By this means it was intended that cicatrification should be allowed to go on, and yet decomposition of the discharge be prevented; and this seemed to be to a great extent, if not entirely, attained.

There was, however, one unfavourable circumstance. The little sore on the outer side of the leg, which had been dressed separately without carbolic acid, and had for some time been observed to be increasing rather than diminishing, now assumed unmistakably the appearance of a mild form of hospital gangrene, and became blended with the main sore. For two days an attempt was made to correct the disease by touching the affected part with nitric acid; but on the eighteenth day it was clear that some more effectual measures must be adopted, as the skin in the vicinity had become insidiously undermined to a very serious extent. Accordingly I placed the boy under chloroform, and scraped away with a spoon all the soft grey sloughs, slitting up the skin in order to gain access to them, and in some parts clipping portions of it away, and then applied the strongest nitric acid thoroughly to the bleeding surface. As the disease extended up to the anterior edge of the crust, I thought it right to examine the state of the parts beneath, and as it was pretty loose I removed it. And now a sight presented itself which filled me with horror. There was, indeed, no appearance of hospital gangrene in the parts which the crust had covered, the granulations there having the florid aspect of perfect health; but in the large sore lay the lower fragment of the tibia, freely exposed

to the extent of two inches and a half in length, bare and white like a macerated bone. At the upper end of this fragment, and apparently for a considerable distance from it, the bone was thus denuded round its entire circumference; and, judging from previous experience, there was reason to expect that, even if the patient should survive the profuse suppuration which was to be anticipated, about two inches of the whole thickness of the tibia must exfoliate, an amount of loss which, in the child's small limb, would of necessity render it utterly useless. The upper fragment was also bare for about half an inch just above its extremity, but the end itself was covered with prominent granulations.

Though despairing of any good result, I resolved to watch for a while the progress of events, prepared to amputate as soon as the boy's health should show signs of failing; and comforting myself with the reflection that he had been brought into a state greatly more favourable for the operation than on his admission. In order to keep down the amount of the discharge the sore was dressed with the sulphite of potash lotion, a poultice being applied to the part which had been treated with nitric acid. When the sloughs caused by the caustic separated a healthy surface appeared, which in the course of the next ten days was nearly healed. In other parts of the sore, however, grey patches occasionally showed themselves, assuming healthy characters after being touched with carbolic acid, which, when efficient, has the advantage over other caustics of being painless. But at length spots of hospital gangrene appeared in a form no longer amenable to this mild treatment, in spite of which they began to extend rapidly, and on the 26th of July it became necessary to put the child under chloroform and apply nitric acid in the same thorough manner as before. This had the effect of producing a perfectly health state of the whole sore, which proceeded to heal with great rapidity; so that by the 8th of August it was found to measure an inch less in length and two inches less in greatest breadth than at the time when the crust was removed.

In the meantime his general health, instead of deteriorating, had improved, and he was evidently regaining flesh, while the

discharge of pus was astonishingly little considering the state of the limb, being barely sufficient to soak the single layer of lint that covered the sore.

The explanation of this satisfactory state of things was afforded by an observation of much interest made at this period. Since the removal of the crust the granulations had been growing up on all sides about the bone, so that the bare part of the upper fragment was almost entirely covered in, and even the lower fragment, which projected beyond the level of the upper, was to a great extent embedded in the new growth. It had been noticed before the end of this fragment was so much covered up, that granulations were sprouting from the medullary canal, showing that the bone was not dead in its entire thickness. Nevertheless, as the superficial parts had certainly lost their vitality, I had not doubted that a thin layer at least must exfoliate from the whole. Now, however, I observed that some of the surface which remained exposed had assumed a pink colour, implying that the layer of dead bone, whatever its thickness might have originally been, had become so thin as to be transparent, through absorption by new tissue growing in the interior. Further, on attempting to pass the eyed end of a probe between the tibia and the granulations which had enveloped it, I found to my surprise that the instrument could only be introduced for a very short distance, the granulations, with the exception of a narrow free border, being everywhere adherent. The new tissue outside the bone had coalesced with that within, after complete absorption of the intervening dead stratum. Hence the remarkable absence of discharge from around the bone.

During the following month I was absent from home, but was informed that the same process was for some time continued: the granulations gradually encroaching more and more on the exposed bone, and adhering to it as they advanced. The upper fragment was thus entirely covered without any exfoliation occurring, and the bare surface of the (p. 359) lower fragment was reduced to comparatively small dimensions. On the 10th of September the remainder of the dead part, being loose, was removed without difficulty as an exfoliation. It was about an

inch in greatest length; but was of extremely irregular shape, full a quarter of the circumference of the tibia being deficient. At the upper end, where it had been most prominent and had become discoloured, it had nearly the full thickness of the dense tissue; but towards the lower end it became thinned away, so as to be in some places as delicate as tissue-paper. The outer surface presented near the margin an appearance of especial interest, being at some parts, even where the bone had considerable thickness, variously scooped and bevelled in a manner that admitted of no other explanation than that the granulations overlapping the dead bone externally had been engaged in its absorption. On applying a magnifier to these excavations in the external surface, they were seen to present a peculiar velvety aspect, differing from the rest of the exterior, but resembling the internal parts of the exfoliation.

The only observation at all analogous to this with which I am acquainted is that of the effects produced upon the ivory pegs used in Dieffenbach's method of treating ununited fracture, the parts of the pegs driven into the bone having been observed, when removed, to have suffered diminution in size. This has hitherto remained as an isolated fact, and it has been regarded as an axiom in surgery that a piece of bone once dead must all come away as an exfoliation. Why it was that in the case before us the osseous tissue destroyed by external violence, aided by the action of carbolic acid, was so exceptionally affected by surrounding parts, the granulations in its vicinity discharging the office of absorbents of the dense tissue, instead of forming pus like those around an ordinary exfoliation, I will reserve for future discussion, when I shall have occasion to point out the great importance of the fact in its bearing both on pathology and practice. Meanwhile I may remark that it illustrates beautifully the function of absorption, which, even where solid substances are taken up, does not require any special set of absorbent vessels, but may be effected even by granulations, the most rudimentary of all tissues, each cell feeding upon any suitable substance in its vicinity.

We also see at once the value of the observation with refer-

ence to the treatment of compound fracture with carbolic acid; for it shows that in cases in which the bone is exposed, the acid may be applied so freely as to cause death of its tissue without necessarily inducing exfoliation.

The case was now reduced to one of simple fracture with a large granulating sore, and this was greatly diminished and healing rapidly, while the union of the fragments was becoming very firm; and the limb would doubtless soon have been entirely sound had it not been for that cruel scourge, hospital gangrene. This, however, had shown itself ten days before the removal of the exfoliation, not in the sore, but about an inch from its edge, as a pustule in the cicatrix, which on bursting disclosed a grey slough that soon showed its characters unmistakably, producing considerable destruction of the scar, although the original sore continued to heal kindly.

I will not enter into the history of this and numerous subsequent attacks of the disease further than to state that they were partial in their effect, the unaffected parts still healing with rapidity, and that they continued to yield to the treatment with nitric acid; so that at one time the whole sore was very nearly healed.

But in the early part of October the disease assumed a more intractable form, and in spite of the most energetic use of nitric acid on several occasions, which produced illusory appearances of temporary improvement, by the 27th of the month the sore had become enlarged to nearly its original dimensions, while the limb had swollen greatly through inflammation caused by the irritation, and the boy's general health was rapidly giving way under the increased discharge and nervous excitement.

The question of amputation now again presented itself, but a good airy room in a different department of the hospital being happily now at my disposal, I determined to give the limb one last chance. Before he was taken to the new ward, nitric acid was once more thoroughly applied. His nurse was directed to change the poultice every three hours, and he continued to take wine and some tonic medicine. His general health immediately improved, and when the slough separated, the sore looked

healthy. It was now dressed with lint dipped in a solution of sulphate of copper, five grains to an ounce of water, and over this a poultice, the whole being changed every three or four hours night and day; and under this treatment cicatrisation proceeded rapidly. Yet when the scar had attained a certain width, a tendency to vesication again showed itself threatening recurrence of the disease, and in order to prevent the newly-formed epidermis from acquiring poisonous qualities as it seemed to do, I ordered the lint with the lotion, as well as the poultice, to be extended over the whole cicatrix. From the time this dressing was adopted the progress was uninterruptedly satisfactory till the 9th of January, when the sore was at length entirely healed, and he was allowed for the first time to put his foot to the ground. The contraction of the large cicatrix, involving at one part the gastrocnemius muscle, had caused some bending of the knee and pointing of the toes. The former has since become corrected spontaneously by his habitual attitude, sitting in bed with the legs extended before him. The pointing of the toes has also become diminished, and will probably soon pass off entirely, without the division of the tendo Achillis, which I had in view. The tibia, which has long been firm, is of precisely the same length as the other, and the contour of the limb is natural. His general health also is excellent; but he was detained in the hospital till the 9th inst. (March, 1867), on account of an obstinate eczematous eruption on the integument of the leg irritated by the long-continued poulticing.

(p. 387) CASE 6.—The following case terminated fatally, but from circumstances of an accidental nature; and I trust that the instruction to be derived from it will not be interfered with by the unhappy ultimate result.

John C—, aged fifty-seven, a labourer, was working in a quarry at Row, near Helensburgh, on the Clyde, at nine A.M. on Oct. 26th, 1866, when, striking with a crowbar an overhanging part, he brought down an enormous mass of stone weighing six or seven tons, which fell in large blocks on and about him. His right thigh-bone was broken in its lower third, and, as afterwards appeared, the end of the upper fragment was driven

through the skin at the inner aspect of the limb a little above the knee. The right collar-bone was fractured at the same time, and he was severely contused in other parts. It was long before his only companion in the quarry could extricate him from his position, and the procuring of a conveyance involved further delay; so that a considerable period elapsed, during which he lost much blood from the thigh, before he could be taken to Helensburgh. Here he was placed on a litter, with a warm moist blanket round the limb, with the object, as he said, of checking the bleeding, which, however, it could not but tend to encourage. He was then conveyed by train to Glasgow, where he reached the infirmary six hours after the occurrence of the accident.

Dr. Archibald Cameron, the house-surgeon, seeing the case to be a very grave one, at once sent for me, but without any delay introduced carbolic acid into the wound by means of a piece of lint held in a pair of dressing forceps, passing by means it about an inch in every direction beneath the integument, after squeezing out a considerable quantity of extravasated blood from the orifice, which was large enough to admit the tip of the finger.

On arriving, an hour after the patient's admission, I found him in a state of prostration sufficiently explained by the severity of his injuries and by the blood lost to the circulation, including a large amount extravasated in the limb, and distending, not only the whole thigh, but the calf, the tenseness of which contrasted strikingly with the flaccidity of the other.

Under these circumstances decomposition of the blood effused among the tissues would have been necessarily fatal. And yet, considering the length of time that had elapsed since the receipt of the injury, and the fact that a reeking flannel had been for two hours in contact with the wound, and had already a somewhat offensive odour when removed from it, there seemed but a poor chance for the treatment with carbolic acid. On the other hand, taking into account the man's time of life and general condition, I believed that to amputate through the thigh infiltrated with blood would be certainly to kill him. And therefore,

as it was impossible to say that the other treatment had no chance, while, if it should prove successful, it would have the immeasurable superiority of saving limb as well as life, I determined to persevere with it.

Having removed from the wound the dressing placed on it by Dr. Cameron, I forcibly squeezed out a further large amount of blood, and applied carbolic acid in lint and also mixed with blood, so as to provide for a crust of considerable thickness overlapping the skin by about half an inch every way. This was covered with a circular piece of tin, two inches across, well bulged out except a flat margin about a quarter of an inch wide, which rested on the surrounding integument. This tin cap was retained in position by a single turn of bandage tied round the limb.

The lower end of the upper fragment was much displaced downwards in the vicinity of the wound, but returned towards its natural position on extension of the limb. There still remained considerable depression anteriorly over the seat of fracture; but the lower fragment did not seem to project towards the ham so much as to forbid the use of the long splint. This I accordingly employed with two interior splints to support the muscles of the thigh, one of Gooch's material on the outer aspect, the other a large sheet of stout block tin, embracing the anterior, inner, and posterior aspects of the limb to a little below the knee, padded in the first instance with a dry towel, for which a hot fomentation should be substituted when all tendency to hemorrhage should have ceased. The object of having the tin extend round the back of the thigh was that it might prevent the discharges from soaking into the bed beneath; and in this way it proved extremely useful.

He passed an uneasy though not entirely sleepless night, suffering more from his shoulder and bruised side than from the thigh. Next morning his aspect was favourable, the pulse 76, and tongue natural; he took a little tea for his breakfast, but nothing solid. The tin cap having been removed, care being taken to avoid detaching the crust along with it, carbolic acid was applied to the surface of the latter. A hot fomentation

cloth was then placed on the inner side and front of the thigh and gave him great comfort, and when the dressing was completed he was quite easy. The interior splints being kept in position by looped bandages, and the long splint by the usual folded sheet fixed by pins, along with the perineal band and handkerchief round the foot, the fomentations could be changed night and morning without any disturbance of the limb.

The following night he had a good deal of sleep, the thigh not causing him any inconvenience; and next day, the third after the accident, he took solid food with relish. His pulse was 72, and his tongue continued moist, though he was somewhat thirsty. The crust was touched again with carbolic acid, and covered with a circular piece of calico to prevent the tin cap from adhering to it. He still found comfort in the fomentations.

On the fourth day he made a substantial breakfast after a good night's rest, and was not so thirsty. There was, however, now seen for the first time a slight blush of redness on the front of the thigh over the seat of injury. This was on the fifth day somewhat increased, and the thigh and calf were both more swollen. The tongue also was slightly furred at the base, and his appetite was not quite so good.

On the sixth day the dimensions and appearance of the limb were unaltered, but on the seventh both the redness and swelling were distinctly diminished.

By the end of the second week his appetite was improved and his pulse was 76; while there had not been a drop of discharge from beneath the crust, which had been still touched daily with carbolic acid, the fomentations also having been continued. The swelling, however, had not subsided, and the redness, though varying in extent and degree, had never disappeared from over the seat of fracture. On the fifteenth day a defined prominence made its appearance at this part in a space about as large as the palm of the hand, a little further forward than the crust, and a sense of fluctuation was to be perceived in it. In the evening Dr. Cameron, on changing the (p. 388) fomentation, saw more pus than he thought could be accounted for by the superficial excoriation round the crust, and next morning, on

removing the flannel, I found it soaked with similar discharge; a considerable quantity also lying between the tin splint and the limb. On raising the tin cap, the matter was seen welling out from beneath the lower edge of the crust. It was perfectly free from odour, confirming the conclusion I had previously arrived at that this abscess was not in any way caused by decomposition from atmospheric influence. The long period that elapsed before it made its appearance, together with the absence of any serious constitutional disturbance, clearly showed that the carbolic acid had effectually answered the purpose for which it was applied, the constant oozing of blood from the small wound having doubtless been in the patient's favour, by preventing decomposition from penetrating far into the interior before he came under treatment. We know that a mass of extravasated blood occasionally becomes the seat of suppuration without the existence of any external wound. A curious instance of this occurred lately in my practice, in a boy who fell down the hold of a ship upon his head, and, besides serious cerebral symptoms, exhibited at once a remarkable prominence of the right eyeball, evidently due to extravasation of blood into the orbit. There being no wound, I expected that the blood would be absorbed; but after the lapse of several days, the prominence of the eye showed increase rather than diminution, and the boy began to complain of supraorbital pain. Fluctuation then became perceptible, and pus was evacuated by incision, after which the eyeball gradually resumed its natural position.

Such I supposed to be the nature of the abscess in C——'s case, and previous experience made me fear that, if decomposition of its contents should occur, the irritation of the fetid pus might cause very serious consequences from rapid extension of suppuration among the imperfect and feeble products of the organisation of the blood in the yet swollen limb.

Hence I had intended to evacuate the matter by aid of carbolic acid in such a way as to prevent decomposition. As the abscess was not near the surface at the part where it appeared to be pointing, I had reckoned on having plenty of time for my operations, and was greatly disappointed to find that it had discharged itself spontaneously.

Nevertheless, as the pus was proceeding from beneath the crust impregnated with carbolic acid and was still quite odourless, I did not altogether despair of attaining my object. In order to make the crust more effectual, I extended it for about three-quarters of an inch at the part from which the pus was escaping, by a piece of lint dipped in carbolic acid, which, when mixed with pus, forms a sort of curdy mass which answered pretty well for a crust. A considerable quantity of matter, of moderate consistence and greenish white colour, was then pressed out from the limb. A new tin cap having been made, large enough to cover the whole of the extended crust, the fomentation was continued as usual.

Next day it was evident, from the sense of fluctuation, that reaccumulation had occurred in the abscess, but no further discharge had taken place. On removing the tin cap, however, pus was seen to well out from a new situation at the upper edge of the crust. A piece of lint dipped in carbolic acid was at once placed on this part, and the matter was pressed out and carefully collected, measuring 3 oz., of moderate consistence and yellowish white colour, still without odour except that of carbolic acid. The crust having been somewhat extended at the situation of the new opening, the whole was freely treated with carbolic acid, the tin cap readjusted, and fomentation continued.

During the rest of the week that followed the first evacuation of the abscess the same treatment was pursued with the most satisfactory results. Some pus was usually seen on the fomenting flannel both morning and evening, and some was pressed out of the limb from the orifice last formed, but the amount rapidly diminished in quantity, and also became thinner and more transparent, while it continued free from odour. It may be worth while to mention in detail the quantities obtained from the limb in the morning of each of these days. On the seventeenth day it was an ounce and a half, somewhat thinner than before; on the eighteenth, two drachms and a half, decidedly thinner; on the nineteenth, half a drachm, much thinner and more transparent; on the twentieth, a quarter of a drachm, similar in quality, and on the twenty-first, six drops only, and almost free

from opacity. Finally, in the evening of that day no discharge was seen on the flannel, nor could any be squeezed out from the limb. Meanwhile the calf, which had increased markedly in circumference just before the abscess opened, steadily diminished, and in the thigh all swelling disappeared from over the seat of fracture, so that the end of the upper fragment, previously quite obscured, could be distinctly defined. His general health, too, had improved; his tongue had become quite clean, and he had acquired for the first time since his admission a genuine appetite, the pulse continuing about 72.

I suspect, however, that this success made us relax a little our vigilant care in guarding against decomposition. But be this as it may, the method which we pursued in order to avoid it was not, as experience has since shown, thoroughly trustworthy. Would that I had at that time known of the mode of proceeding which will be found described in a future section of this communication. Very different then might have been the issue of the case!

On the twenty-second day pus was again found in the flannel, and some bubbles of gas were observed to escape along with the two or three drops that could be squeezed from the limb, and these had a distinctly offensive odour. Judging it now useless to retain the crust any longer I removed it, and found the original wound still sealed by the original clot, the openings by which the pus had escaped being new apertures in the skin overlapped by the crust. In the after part of the day he had a good deal of uneasiness, and in the evening half an ounce of pus, with numerous air-bubbles, was pressed out of the limb by Dr. Cameron. After this the patient passed a comfortable night, and in the morning only two drachms of matter could be procured from the thigh, but this was thicker and more opaque than it had been, with decidedly offensive odour, and contained bubbles of gas; there was also pus in the flannel. There was, further, some return of welling over the seat of fracture.

But though the plan of dealing with the abscess had failed to accomplish all that I desired, its essential object appeared to have been attained. For during the week in which decomposi-

tion was prevented, the thigh had become so much consolidated and strengthened that all danger of serious consequences seemed to have been tided over. No extension of the suppuration took place beyond the trifling degree above described, and his constitution did not suffer. Any further use of carbolic acid being obviously uncalled for, the sore was simply dressed with a lotion, the lint being so arranged as to allow free escape for the pus, and afterwards, to promote this more effectually, a small perforated caoutchouc tube was introduced, a dry cloth being substituted for the fomentation. Under this management the discharge gradually diminished in quantity, and became again thinner and more transparent, and the swelling of the calf became steadily reduced.

Still the opening did not close, and on the 2nd of December, more than a fortnight having passed in this way, I introduced a probe, and found that it passed downwards to bare bone, including a considerable extent of surface in the lower fragment. Here, then, was presented the prospect of a tedious process of exfoliation; whereas if decomposition of the pus had not occurred, the granulations would probably have closed upon the dead bone, and absorbed it, as in the last case, and the fact that any part had lost its vitality would then never have been known. That there is a reasonable ground for this belief will, I trust, appear from the discussion in the succeeding section.

For a long time the progress of the patient continued satisfactory, the process of union of the fragments advancing steadily, till in the early part of February, the bone being firm, the splints were entirely discarded, and the case was reduced from one of fracture to one of limited exfoliation. It was satisfactory also to find that the knee-joint continued movable, so that I confidently anticipated recovery, with a perfectly useful limb.

At this period, however, a new symptom presented itself—viz., hemorrhage from the sinus. Mr. Hector Cameron, my present house-surgeon, who saw the first appearance of bleeding, supposed it to proceed from the surface of the granulations; for it was then small in amount, and ceased spontaneously. Some days later, however—viz., on the 11th of February,—a very

profuse hemorrhage occurred, the blood soaking through the bed, and dropping upon the floor beneath, before it was observed, and the gentleman who was summoned to see the patient in Mr. Cameron's absence, found him pulseless. He afterwards rallied to some extent, but remained utterly prostrated, and unable to retain the slightest nourishment. As the popliteal artery could be felt beating in the lower part of the ham, I hoped that the source of the blood might be some minor branch, which might possibly close. But it afterwards appeared that a circular opening existed in the main vessel, occasioned no doubt by the pressure of an irregular projection of the lower fragment. It would be irrelevant to relate particularly the history of his yet further exhaustion by recurrent hemorrhages after delusive temporary cessations, or of my attempts to restore him by tying the popliteal artery, and making arrangements for transfusion, to which he declined to submit. He died on the 25th of February.

(p. 507) The next four cases occurred in the practice of my colleagues in the infirmary, who have kindly placed them at my disposal.

CASE 7.—Mary M——, aged sixty-two, was admitted under the care of Dr. Morton on August 13th, 1866, at eleven P. M., when she stated that about five o'clock in the afternoon of that day she missed her footing when going down stairs, and fell with violence, and on getting up found that her right forearm was broken and bleeding. A medical man was called in, who made various applications in order to stop the hemorrhage, but failed to do so, and she was advised to go to the infirmary. Mr. A. T. Thompson, the house-surgeon (to whom I am indebted for notes of the case), on removing the bandage, from which blood was trickling, found both bones of the forearm broken a little above the wrist, and a detached fragment of the radius projecting from a wound about as large as a fourpenny-piece, on the outer aspect of the limb. Having extracted this fragment, he applied liquid carbolic acid thoroughly to the interior of the wound. This rather increased the bleeding, which, however, he arrested completely by plugging the orifice with a bit of lint

dipped in the acid. Over this he placed a mixture of blood and carbolic acid, covering it with a piece of dry lint. He then put up the limb in two well-padded Gooch's splints, retained in position with a continuous bandage. The apparatus was left undisturbed for five days, when, on removal of the splints, it was found that the piece of dry lint over the wound, though it had been saturated with blood, was quite dry, having become incorporated with the crust beneath. It was not interfered with except that the surface was touched with carbolic acid, and the splints were reapplied as before, the part being quite free from uneasiness.

On the twelfth day the splints were again removed and the crust was detached, when it was found that the piece of lint with which the wound had been plugged had become partly pushed out of the orifice. The plug also was now removed, when the surface beneath was observed to be granulating, but entirely free from pus. The sore was dressed with one part of carbolic acid to seven parts of olive oil applied on lint every second day, the use of the splints being continued till the 8th of September, when she was discharged, with the sore healed and both bones firmly united, two days less than four weeks after the accident.

This case is valuable as an example of a mode in which troublesome bleeding in compound fracture may sometimes be advantageously arrested. The entire absence of pus about the plug on the twelfth day after its introduction contrasts strikingly with the suppuration invariably caused within four days by a piece of lint inserted without carbolic acid into a wound.

CASE 8.—Samuel B——, aged thirteen, was admitted under Dr. Morton's care, on Aug. 30th, 1866, with a compound fracture of the left femur, about the junction of the upper and middle thirds of the shaft, and a simple fracture of the right thigh in a similar situation. He started that about four hours previously he was engaged in some work about a steam-engine, when he was struck by one of the balls of the "governor," and hurled with great force against an iron pillar. The men who brought him to the infirmary said that when he was raised from the ground a piece of bone was seen to protrude from a wound in the left

thigh, but was restored to its natural position by a medical man who was called in to see him, and who applied a long splint and bandage to each limb. Mr. A. T. Thomson, on examining the boy, found a lacerated wound about three inches long at the upper part of the left thigh, running transversely from the middle of the inner side of the limb to its posterior aspect, and in this wound the upper fragment of the femur was visible, somewhat displaced, but not protruding. There was some bleeding, but not to any serious extent. He sponged out the wound thoroughly with a solution of one part of carbolic acid in three parts of olive oil, and then covered its lips with a mixture of blood and the undiluted acid spread upon lint, and over this a piece of sheet-tin, retained in position by means of a looped bandage. He next corrected the faulty position of the fragments and applied lateral splints of Gooch's material to the thigh, maintaining gentle extension by means of plasters applied to the integument of the leg after the American plan, and fixed to the foot of the bed, a perineal band being attached to the bed-head. While the left limb was thus kept readily accessible for changing the dressings, the long splint was employed as usual for the simple fracture on the right side.

Next day the surface of the crust was touched with carbolic acid, and a hot fomentation applied to the limb.

On the third day the crust was removed through a misunderstanding, but it was resolved to follow out the treatment on the same principle, and with this view the wound was dressed twice a day with lint dipped in the mixture of carbolic acid and oil (one part to three), covered with the tin, as the crust had been before, while the fomentations also were continued. Meanwhile the limb remained free from pain, redness, or swelling, and there was a complete absence of constitutional disturbance.

On the sixth day, however, he was a little feverish, and remained so, though without any apparent local symptoms, till the twelfth day, when Mr. Thomson noticed that the central part of the wound, which had become covered with a whitish crust, was somewhat prominent, and, on careful examination, perceived a distinct sense of fluctuation. He therefore removed

the white layer from that part, when eight ounces of perfectly odourless pus escaped. A probe introduced failed to detect any bare bone. Mr. Thomson now sponged out the cavity of the abscess with the mixture of carbolic acid and oil, and left in it a strip of lint dipped in the same, continuing the other dressings as before. The constitutional disturbance now at once subsided, and under the same dressing the cavity of the abscess quickly contracted, and in a little more than a fortnight closed entirely. Six weeks after the accident the wound was completely healed, and both the thigh-bones were firmly united, with the limbs of equal length. In another week he was able to stand.

This case, which, I cannot avoid remarking, reflects great credit on the house-surgeon in charge, is interesting as another instance of the occurrence of abscess in compound fracture, independently of atmospheric influence. That it was so in this instance is clearly shown by the entire absence of constitutional symptoms for the first five days, the circumscribed character of the suppuration, and the odourless nature of the pus. The injured part suppurated, probably, from the same cause as a severe bruise may without any breach of the integument. The satisfactory results obtained by treating the wound with carbolic acid diluted with oil, instead of the undiluted acid, will naturally suggest the inquiry whether this would not always be the better practice. And I may mention that my former house-surgeon, Dr. A. Cameron, met with similar success in two cases in which he pursued the same treatment—one of them a compound fracture of the ulna at the elbow, the other a severe contused wound of the back of the hand communicating with a fractured metatarsal bone. But considering how much is at stake, and that the patient's life may depend upon entire destruction of the septic germs that lie in the wound, I am inclined to think it wiser to avail ourselves of the full energy of the pure acid, more especially since we have had sufficient evidence that any caustic effects it may have are not productive of serious consequences.

CASE 9.—William C—, aged thirty-three, was admitted on the 29th of September, 1866, under the care of Dr. Eben. Watson, with a compound fracture of the left tibia, produced by an

omnibus passing over the limb at eight o'clock P. M. The broken part of the bone was exposed in a wound six and a half inches in length, a little above the ankle. The skin in the vicinity was detached from the subjacent tissues for about two inches, and there was ecchymosis reaching some distance up the leg, with other evidence of severe contusion.

(p. 508) An hour and a half after the accident Dr. A. Forsyth, the house-surgeon, from whose notes these particulars are obtained, sponged out the wound thoroughly with undiluted carbolic acid, and placed over it layers of calico soaked with the acid; and, in order to provide for a sufficiently substantial crust, spread over the calico some paste composed of starch moistened with carbolic acid, covering the whole with a piece of block-tin secured with a bandage, the fracture being treated with a suitable apparatus. After the dressing, the patient, though unable to express his feelings, being dumb, appeared entirely free from uneasiness.

Next day the tin was carefully removed from the crust, the surface of which was touched with carbolic acid, and, the tin having been readjusted, hot fomentations were applied to the leg and foot. The pulse was now 96, the tongue clean, and the appetite good. The same treatment was pursued till the thirteenth day, when the fomentations were discontinued, and the edges of the crust which were loose were clipped away, and lint moistened with water was applied to the granulating surface thus exposed, the remainder of the crust being still touched daily with carbolic acid. Meanwhile there had been no suppuration beneath the crust, and the patient had remained free from constitutional symptoms.

On the seventeenth day the crust, which had separated from the wound at its lower third, was removed, disclosing a healthy granulating surface, the bone being nowhere visible, while there was no appearance of pus, except a trifling amount towards the lower part. The sore, which was entirely superficial, was now treated like an ordinary ulcer, and healed quickly. The bone also united as in a simple fracture, and he was discharged eight

weeks after the receipt of the injury, having been kept longer in the hospital than would otherwise have been necessary, on account of a head affection to which he was subject.

The above case, besides being a good example of the effects of the treatment of compound fracture with carbolic acid, affords an illustration of a practice which I have on several occasions found useful when there has been but little bleeding from the wound, a dough or paste composed of flour or starch, moistened with the acid, being employed in lieu of the compound with blood to render the crust sufficiently substantial.

CASE 10.—Thomas M'B——, a labourer, who gave his age as fifty-two, but had the appearance of a much older person, was admitted at noon on the 2nd of January, 1867, under the care of Dr. G. Buchanan, having been knocked down an hour before by the shaft of a luggage wagon, the wheel of which passed over his left leg, producing a compound fracture in the lower third of the limb. Mr. James Robinson, the house-surgeon who has given me notes of the case, found a wound from which blood was oozing, about an inch and a half in length, exposing part of the tibia, and communicating with the seat of fracture. The tissues were pretty severely contused. Undiluted carbolic acid was applied freely to the interior of the wound by means of lint held in a pair of dressing forceps, and a crust was formed of blood mingled with the acid, covered with lint, over which a cap of tin was placed, well bulged out to correspond to the substantial crust, and large enough to overlap to a slight extent the sound skin in the vicinity. The fragments having been brought into proper position, the limb was put up with lateral wooden splints, with a hot fomentation. At the conclusion of the dressing the patient expressed himself as greatly relieved. The pulse was then 65.

Next day he was free from pain after a fair night's rest. The pulse was 74, and the tongue clean and moist. The surface of the crust was touched with carbolic acid, the limb being still fomented; and the same treatment was continued daily for the following fortnight, during which the limb was entirely free from pain, redness, or suppuration, while his constitution was quite

unaffected by the injury, the tongue remaining clean, and the pulse varying only between 72 and 85.

I was present when the crust was removed, eighteen days after the accident. Not a drop of pus existed beneath it. On the contrary, the superficial sloughs of the cutis occasioned by the caustic action of the acid first applied remained still undetached. The exposed surface was treated with water-dressing, and in two days presented the appearance of an ordinary granulating sore, which healed without interruption. Six weeks and three days after the receipt of the injury the splints were removed, the bones being satisfactorily united.

This is an excellent example of the effects of the carbolic-acid treatment in a compound fracture of the leg of average severity. No simple fracture could have caused less disturbance, either local or constitutional.

CASE II.—The following case, though incomplete, is given on account of the conclusive evidence it affords regarding a complication of compound fracture of much interest both practically and theoretically—viz., emphysema of the limb in consequence of air being introduced into the wound, and diffused among the interstices of the tissues by a pumping action of the fragments of the broken bone when freely moved through restlessness of the patient or carelessness of his attendants before he comes under the surgeon's care. Such a state of things may seem at first sight to render it impossible to prevent decomposition of the extravasated blood, since it would be out of the question to attempt to apply carbolic acid to all the emphysematous tissues. But I have long indulged the hope that, the air entering in small successive portions, its floating organisms might be arrested by the first blood with which they came in contact, and remain for some time confined to the vicinity of the external wound, in which case, by squeezing out as much blood as possible from the orifice in the integument, and introducing carbolic acid freely, we might get rid of all causes of decomposition in the limb, the mere atmospheric gases diffused more remotely, however abundant, being entirely innocuous. This hope, it now appears, was not ill-founded.

John D—, aged fifty-five, a calico-printer, of intemperate

habits, was admitted under my care in the Royal Infirmary at six P. M. on the 4th of April, 1867, having broken both bones of his right leg about an hour before by jumping out of a window into the street, from a height of between fifteen and twenty feet, while in a state of intoxication. He was carried up-stairs to his lodgings, kicking about in his drunken frenzy. A cloth was then put round the leg, but no efficient means were employed to steady it, and he was conveyed to the hospital from a distant part of the city in a cab, moving the limb recklessly during the whole journey. His friends stated that he had lost a great deal of blood, and the cloth which was round the limb on his admission was saturated. Mr. H. Cameron, the house-surgeon, found a wound about half an inch in length, situated over the spine of the tibia, at the junction of the middle and lower thirds of the bone, the fracture being half an inch lower down, and obviously communicating. The wound was bleeding very freely, and the leg was considerably swollen through extravasation of blood into it. On manipulation, Mr. Cameron found the tissues about the seat of fracture emphysematous, the characteristic crackling sensation being experienced fully four inches above the wound and two inches below it, and also on the opposite side of the limb, over the fibula; and as a result of the handling, a frothy mixture of blood and air, in larger and smaller bubbles, escaped from the orifice. The fragments were much displaced, the foot being greatly everted.

Mr. Cameron, having squeezed out as much blood as possible from the wound, introduced melted crystallised carbolic acid in a piece of calico held in dressing-forceps, which he passed in various directions for more than two inches beneath the integument and about an inch and a half among the deeper structures of the limb, using three different pieces of calico soaked with the acid, and leaving the last in the wound as a plug to check the very free hemorrhage, which the treatment had considerably increased. He then applied several layers of calico steeped in carbolic acid and smeared with blood, so as to make a pretty thick crust overlapping the skin by about half an inch, and adapted to the crust a cap of block-tin of slightly larger dimensions, pressing it down upon the skin by means of a looped

bandage encircling the leg. Having next corrected the displacement of the fragments, he moulded a pasteboard splint to the outer side of the leg and foot, strengthening it with a temporary Gooch's splint, and laid the limb on its outer side upon a pillow with the knee bent. The patient now stated that the pain he had suffered was greatly relieved. His pulse was 100. Two hours later, as a good deal of oozing of blood was still going on, a folded cloth was placed upon the tin cap and pressed down upon it with a bandage. The limb meanwhile was considerably more swollen, from bleeding into its interior, kept up, no doubt, by the sudden jerking movements which in his unreasoning condition he could not be prevented from making. The pressure employed greatly diminished the external hemorrhage, but did not entirely arrest it; and when two hours more had elapsed Mr. Cameron asked my advice. I recommended the use of a well-fitting internal splint, to procure greater steadiness of the fragments, and so get rid of the irritation which perpetuated the bleeding. Mr. Cameron, however, on removing the compress, found that all tendency to oozing of blood had ceased. The patient was now sober, but continued very restless. The internal splint was therefore applied, and thirty drops of solution of muriate of morphia were administered.

(p. 509) During the night he suffered a good deal, and got no sleep at all. Next morning, however, he complained rather of a general sense of weariness and sickness, the consequences of his debauch, than of pain; the pulse had fallen to 76; and he took his breakfast pretty well. The surface of the crust was touched with carbolic acid, and this was repeated in the afternoon, when a hot fomentation was applied to the inner side of the leg, and over this a sheet of stout block-tin, to serve, as in some previous cases, the double purpose of ensuring the efficiency of the fomentations, and acting as an internal splint. The limb was now quite easy. At night the pulse was still 76. He had made a pretty hearty supper, and felt only occasional twinges in the limb. The fomentation was changed, and the crust again touched with carbolic acid, and the opiate repeated.

He passed the following night like the preceding, without getting any sleep whatever; and in the morning his pulse was 90,

although the limb was free from pain or inflammatory blush, and he made a hearty breakfast. Fearing the approach of traumatic delirium, I ordered a larger opiate to be given at night. Fifty drops of the morphia solution were accordingly administered; and after this dose he slept for about five hours. Nevertheless, he grew more restless, and was found in the morning with the leg fully extended and resting on the calf instead of on its outer side. His pulse continued at 90; and although the state of the limb and his appetite were all that could be wished, he exhibited in the afternoon unmistakable signs of delirium tremens, jerking out his tongue when asked to show it, twitching his hands in an excited manner, and declaring that his bedclothes were creeping away from him, while the restless movements of the limb were continued. I ordered a dose of castor oil, to be followed, as soon as it should have operated, by a drachm of the solution of muriate of morphia, to be repeated if necessary. He took the opiate about eight o'clock P. M., and soon afterwards dozed a little; and at eleven his pulse had fallen to 82. After this he fell into a sound sleep, from which he did not wake until six A. M.; and from this time forth he was perfectly tranquil and rational.

It is needless to enter into particulars regarding his subsequent progress further than to say that it has been in all respects satisfactory; and on the tenth day after the accident, when I saw him last, his pulse was 76, his appetite excellent, and he had the appearance of a man in perfect health. The limb was still free from pain, while the swelling due to extravasation of blood had disappeared, and the skin was of natural aspect. After the second day from the accident, there had not been even any discharge of serum from beneath the crust, which had been daily touched with carbolic acid, the fomentations being also continued, as he found them comfortable.

I need not hesitate to say that all danger in this case is over; and that the compound fracture is already converted into a simple one under circumstances which, even for a simple fracture, would have been trying.

In revising the proof, after nine days more have elapsed. I may add that all has continued to go on well.

PRELIMINARY NOTICE ON ABSCESS

Vol. 2, p. 95

In anticipation of the more detailed account which I hope will soon appear in *The Lancet*, I will now give a description of a new method of treating abscess, which has afforded results so satisfactory that it does not seem right to withhold it longer from the profession generally.

It is based, like the treatment of compound fracture,* on the antiseptic principle, and the material employed is essentially the same—namely, carbolic acid, but differently applied in accordance with the difference of the circumstances. In compound fracture there is an irregular wound, which has probably been exposed to the air for hours before it is seen by the surgeon, and may therefore contain in its interstices the atmospheric germs which are the causes of decomposition, and those must be destroyed by the energetic application of the antiseptic agent. In an unopened abscess, on the other hand, as a general rule, no septic organisms are present, so that it is not necessary to introduce the carbolic acid into the interior. Here the essential object is to guard against the introduction of living particles from without, at the same time that a free exit is afforded for the constant discharge of the contents. The mode in which this is accomplished is as follows:—

A solution of one part of crystallised carbolic acid in four parts of boiled linseed oil having been prepared, a piece of rag from four to six inches square is dipped in the oily mixture, and laid upon the skin where the incision is to be made. The lower edge of the rag being then raised, while the upper edge is kept from slipping by an assistant, a common scalpel or bistoury dipped in the oil is plunged into the cavity of the abscess, and an opening about three-quarters of an inch in length is made, and the instant the knife is withdrawn the rag is dropped upon the skin as an antiseptic curtain, beneath which the pus flows out into a vessel placed to receive it. The cavity of the abscess is firmly pressed, so as to force out all existing pus as nearly as may be (the old fear of doing mischief by rough treatment of the pyogenic membrane being quite ill-founded); and if there be much oozing of blood, or if there be a considerable thickness of parts between the abscess and the surface, a piece of lint dipped in the antiseptic oil is introduced into the incision to check bleeding and prevent primary adhesion, which is otherwise very apt to occur. The introduction of the lint is effected as rapidly as may be, and under the protection of the antiseptic rag. Thus the evacuation of the original contents is accomplished with perfect security against the introduction of living germs. This, however, would be of no avail unless an antiseptic dressing could be applied that would effectually prevent the decomposition of the stream of pus constantly flowing out beneath it. After numerous disappointments, I have succeeded with the following, which may be relied upon as absolutely trustworthy. About six teaspoonfulls of the above-mentioned solution of carbolic acid in linseed oil are mixed up with common whitening (carbonate of lime) to the consistence of a firm paste, which is in fact glazier's putty with the addition of a little carbolic acid. This is spread upon a piece of sheet block tin about six inches square; or common tinfoil will answer equally well if strengthened with adhesive plaster to prevent it from tearing, and in

* See *The Lancet* of March 16th, 23rd, and 30th, and April 27th of the present year.

some situations it is preferable, from its adapting itself more readily to the shape of the part affected. The putty forms a layer about a quarter of an inch thick; it may be spread with a table-knife, or pressed out with the hand, a towel being temporarily interposed to prevent the putty from sticking to the hand or soiling the coat-sleeve. The tin thus spread with putty is placed upon the skin so that the middle of it corresponds to the position of the incision, the antiseptic rag used in opening the abscess being removed the instant before. The tin is then fixed securely by adhesive plaster, the lowest edge being left free for the escape of the discharge into a folded towel placed over it and secured by a bandage. This dressing has the following advantages: . . . The tin prevents the evaporation of the carbolic acid, which escapes readily through any organic tissue such as oiled silk or guttapercha. The putty contains the carbolic acid just sufficiently diluted to prevent its excoriating the skin, while its substance serves as a reservoir of the acid during the intervals between the dressings. Its oily nature and tenacity prevent it from being washed away by the discharge, which all oozes out beneath it as fast as it escapes from the incision; while the extent of the surface of the putty renders it securely antiseptic. Lastly, the putty is a cleanly application, and gives the surgeon very little trouble; a supply being daily made by some convalescent in an hospital, or in private practice by the nurse or a friend of the patient; or a larger quantity may be made at once, and kept in a tin canister. The dressing is changed, as a general rule, once in twenty-four hours; but if the abscess be a very large one, it is prudent to see the patient twelve hours after it has been opened, when, if the towel should be much stained with discharge, the dressing should be changed, to avoid subjecting its antiseptic virtues to too severe a test. But after the first twenty-four hours, a single daily dressing is sufficient. The changing of the dressing must be methodically done, as follows:—A second similar piece of tin having been spread with the putty, a piece of rag is dipped in the oily solution, and placed on the incision the moment the first tin is removed. This guards against the possibility of mischief occurring during the cleansing of the skin with a dry cloth and pressing out any discharge which may exist in the cavity. If a plug of lint was introduced when the abscess was opened, it is removed under cover of the antiseptic rag, which is taken off at the moment when the new tin is to be applied. The same process is continued daily till the sinus closes.

The results of this treatment are such as correct pathological knowledge might have enabled us to predict. The pyogenic membrane has no innate disposition to form pus, but does so only because it is subjected to some preternatural stimulus. In an ordinary abscess, whether acute or chronic, the original cause that led to suppuration is no longer in operation, and the stimulus that determines the continued pus formation is derived from the presence of the pus pent up in the interior. When an abscess is opened in the ordinary way this cause of stimulation is removed, but in its place is substituted the potent stimulus of decomposition. If, however, the abscess be opened antiseptically, the pyogenic membrane, freed from the operation of the previous stimulus without the substitution of a new one, ought, according to theory, to cease to suppurate, while the patient should be relieved from any local or general disturbance caused by the abscess, without the risk of irritative fever or hectic.

Such, accordingly, is the fact. Abscesses of large size have, after the original contents have been evacuated, furnished no further pus whatever, the discharge

being merely serum, which in a few days has amounted only to a few drops in the twenty-four hours. Whether the opening be dependent or not is a matter of perfect indifference, the small amount of unirritating fluid being all evacuated spontaneously by the rapidly contracting pyogenic membrane. At the same time, we reckon with perfect certainty on the absence of all constitutional disturbance.

As an illustration, I may mention the last case which has come under my care. It is that of a young woman, twenty-five years old, with psoas abscess, which had of late been rapidly on the increase, and caused a large swelling below Poupart's ligament, communicating with a fluctuating mass, dull on percussion, reaching to a considerable distance up the abdomen, the femoral vessels being raised over the communication between them. Six days ago I opened, in the manner above described, the swelling in the thigh at the anterior part of the limb where it was nearest the surface, giving exit to twenty-seven ounces of pus, thin, but containing numerous large curdy masses. I introduced a piece of lint, dipped in the carbolic acid and oil, into the incision; and this prevented any discharge from escaping during the next twenty-four hours, (p. 96), when, on removal of the plug of lint under an antiseptic rag, three ounces of turbid serum escaped. For the next three days there was scarcely any discharge, the deeper parts of the incision having cohered. On firm pressure, however, the product of seventy-two hours escaped, and amounted to four drachms of serum. Meanwhile the girl's general health, which had not been interfered with by the abscess, continued perfectly good, neither pulse, tongue, appetite, nor sleep having been disturbed.

In this case, though there is no deformity of the spine, there is great probability that caries of the vertebrae is present. But even though such be the case, there is good reason to hope for a favourable issue. Regarding caries as merely the suppurative stage of chronic inflammation in a weak form of tissue, I have been not surprised, though greatly rejoiced, to find that it exhibits the tendency of inflammatory affections generally—viz., a disposition to spontaneous cure on the withdrawal of irritation. Hitherto, in surgical practice, caries has had to contend against the formidable irritation of decomposing matter, which, under circumstances of weakness, is often sufficient to cause ulceration, even in the soft parts; yet, in spite of this irritation, caries is often recoverable in the child where the vital powers of all the tissues are stronger. If, therefore, this serious complication can be avoided, there seems nothing in theory against the probability that caries may prove curable in the adult. And even should portions of necrosed bone be present, as is not unfrequently the case, our experience of the treatment of compound fracture with carbolic acid has taught us that dead bone, if undecomposed, not only fails to induce suppuration in its vicinity, but is liable to absorption by the granulations around it.*

Such were the hopes which I ventured to express several months ago to my winter class. Since that time I have opened numerous abscesses connected with caries of the vertebrae, the hip, knee, ankle, and elbow, and in all cases I have found the discharge become in a few days trifling in amount, and in many it has ceased to be puriform after the first twenty-four hours. Finally, three days ago—viz., on the 4th inst., (July, 1867), I had the inexpressible happiness of finding the sinus soundly closed in a middle-aged man, in whom I opened in February last a psoas

* See The Lancet of March 23rd, p. 359.

abscess, proved to be connected with diseased bone by the discharge, on one occasion, of an osseous spiculum. For months past we had persevered with the antiseptic dressing, although the discharge did not amount to more than a drop or two of serum in the twenty-four hours, well knowing by bitter experience that so long as a sinus existed the occurrence of decomposition might produce the most disastrous consequences; and at length our patience has been crowned with success.

Hence I no longer feel any hesitation in recommending the early opening of such abscesses, because, while they remain unopened, the disease of the bone is necessarily progressive, whereas when opened antiseptically, there is good ground to hope for their steady, though tedious, recovery.

The putty of the strength above recommended, though it generally fails to excoriate the skin, sometimes produces this effect when long continued. In such case it may be reduced in strength so that the oil contains only one part to five or six without disadvantage when the discharge is very small in amount.

The application prevents the occurrence of cicatrization in the little sore caused by the incision, and perpetuates a trifling discharge from it. Hence it is impossible to judge whether or not the sinus has closed, except by examining it from time to time with a probe, which should be dipped in the antiseptic oil, and passed in between folds of the antiseptic rag. This may seem a refinement, but if we could see with the naked eye a few only of the septic organisms that people every cubic inch of the atmosphere of an hospital ward, we should rather wonder that the antiseptic treatment is ever successful than omit any precautions in conducting it.

The putty used in treating abscesses has proved very valuable in simplifying the treatment of compound fracture, and enlarging the range of its applicability, and also in dealing with incised wounds on the antiseptic principle. But I must defer a notice of these matters to a future occasion.

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On the Antiseptic Principle in the Practice of Surgery^{*}

BY

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IN THE course of an extended investigation into the nature of inflammation, and the healthy and morbid conditions of the blood in relation to it, I arrived, several years ago, at the conclusion that the essential cause of suppuration in wounds is decomposition, brought about by the influence of the atmosphere upon blood or serum retained within them, and, in the case of contused wounds, upon portions of tissue destroyed by the violence of injury.

To prevent the occurrence of suppuration, with all its attendant risks, was an object manifestly desirable; but till lately apparently unattainable, since it seemed hopeless to attempt to exclude the oxygen, which was universally regarded as the agent by which putrefaction was effected. But when it had been shown by the researches of Pasteur that the septic property of the atmosphere depended, not on the oxygen or any gaseous constituent, but on minute organisms suspended in it, which owed their energy to their vitality, it occurred to me that decomposition in the injured part might be avoided without excluding the air, by applying as a dressing some material capable of destroying the life of the floating particles.

^{*} A paper read before the British Medical Association in Dublin on the 9th of August, 1867.

Upon this principle I have based a practice of which I will now attempt to give a short account.

The material which I have employed is carbolic or phenic acid, a volatile organic compound which appears to exercise a peculiarly destructive influence upon low forms of life, and and hence is the most powerful antiseptic with which we are at present acquainted.

The first class of cases to which I applied it was that of compound fractures, in which the effects of decomposition in the injured part were especially striking and pernicious. The results might have been such as to establish conclusively the great principle, that *all the local inflammatory mischief and general febrile disturbance which follow severe injuries are due to the irritating and poisoning influence of decomposing blood or sloughs*. For these evils are entirely avoided by the antiseptic treatment, so that limbs which otherwise would be unhesitatingly condemned to amputation may be retained with confidence of the best results.

In conducting the treatment, the first object must be the destruction of any septic germs which may have been introduced into the wound, either at the moment of the accident or during the time which has since elapsed. This is done by introducing the acid of full strength into all accessible recesses of the wound by means of a piece of rag held in dressing forceps and dipped in the liquid.* This I did not venture to do in the earlier cases; but experience has shown that the compound which carbolic acid forms with the blood, and also any portions of tissue killed by its caustic action, including even parts of the bone, are disposed of by absorption and organisation, provided they are afterwards kept from decomposing. We are thus enabled to employ the antiseptic treatment efficiently at a period after the occurrence of the injury at which it would otherwise probably fail. Thus I have now under my care in the Glasgow Infirmary a boy who was admitted with compound fracture of the leg as late as eight and a half hours after the accident, in whom never-

* The addition of a few drops of water to a considerable quantity of the crystallised acid induces it to assume permanently the liquid form.

theless all local and constitutional disturbance was avoided by means of carbolic acid, and the bones were firmly united five weeks after his admission.

The next object to be kept in view is to guard effectually against the spreading of decomposition into the wound along (p. 354) the stream of blood and serum which oozes out during the first few days after the accident, when the acid originally applied has been washed out, or dissipated by absorption and evaporation. This part of the treatment has been greatly improved during the last few weeks. The method which I have hitherto published* consisted in the application of a piece of lint dipped in the acid, overlapping the sound skin to some extent, and covered with a tin cap, which was daily raised in order to touch the surface of the lint with the antiseptic. This method certainly succeeded well with wounds of moderate size; and, indeed, I may say that in all the many cases of this kind which have been so treated by myself or my house-surgeons, not a single failure has occurred. When, however, the wound is very large, the flow of blood and serum is so profuse, especially during the first twenty-four hours, that the antiseptic application cannot prevent the spread of decomposition into the interior unless it overlaps the sound skin for a very considerable distance, and this was inadmissible by the method described above, on account of the extensive sloughing of the surface of the cutis which it would involve. This difficulty has, however, been overcome by employing a paste composed of common whitening (carbonate of lime) mixed with a solution of one part of carbolic acid in four parts of boiled linseed oil, so as to form a firm putty. This application contains the acid in too dilute a form to excoriate the skin, which it may be made to cover to any extent that may be thought desirable, while its substance serves as a reservoir of the antiseptic material. So long as any discharge continues, the paste should be changed daily; and, in order to prevent the chance of mischief occurring during the process, a piece of rag dipped in the solution of carbolic acid in oil is put on next the skin, and maintained there permanently, care being

* See *The Lancet* for March 16th, 23rd, and 30th, and April 27th, of the present year.

taken to avoid raising it along with the putty. This rag is always kept in an antiseptic condition from contact with the paste above it, and destroys any germs that may fall upon it during the short time that should alone be allowed to pass in the changing of the dressing. The putty should be in a layer about a quarter of an inch thick, and may be advantageously applied rolled out between two pieces of calico, which maintain it in the form of a continuous sheet, that may be wrapped in a moment round the whole circumference of a limb, if this be thought desirable, while the putty is prevented by the calico from sticking to the rag which is next the skin.* When all discharge has ceased, the use of the paste is discontinued, but the original rag is left adhering to the skin till healing by scabbing is supposed to be complete. I have at present in the hospital a man with severe compound fracture of both bones of the left leg, caused by direct violence, who, after the cessation of the sanious discharge under the use of the paste, without a drop of pus appearing, has been treated for the last two weeks exactly as if the fracture were a simple one. During this time the rag, adhering by means of a crust of inspissated blood collected beneath it, has continued perfectly dry, and it will be left untouched till the usual period for removing the splints in a simple fracture, when we may fairly expect to find a sound cicatrix beneath it.

We cannot, however, always calculate on so perfect a result as this. More or less pus may appear after the lapse of the first week; and the larger the wound the more likely is this to happen. And here I would desire earnestly to enforce the necessity of persevering with the antiseptic application, in spite of the appearance of suppuration, so long as other symptoms are favourable. The surgeon is extremely apt to suppose that any suppuration is an indication that the antiseptic treatment has failed, and that poulticing or water-dressing should be resorted

* In order to prevent evaporation of the acid, which passes readily through any organic tissue, such as oiled silk or gutta percha, it is well to cover the paste with a sheet of block tin, or tinfoil strengthened with adhesive plaster. The thin sheet-lead used for lining tea-chests will also answer the purpose, and may be obtained from any wholesale grocer.

to. But such a course would in many cases sacrifice a limb or a life. I cannot, however, expect my professional brethren to follow my advice blindly in such a matter, and therefore I feel it necessary to place before them, as shortly as I can, some pathological principles, intimately connected not only with the point we are immediately considering, but with the whole subject of this paper.

If a perfectly healthy granulating sore be well washed and covered with a plate of clean metal, such as block tin, fitting its surface pretty accurately, and overlapping the surrounding skin an inch or so in every direction, and retained in position by adhesive plaster and a bandage, it will be found, on removing it after twenty-four or forty-eight hours, that little or nothing that can be called pus is present, merely a little transparent fluid, while at the same time there is an entire absence of the unpleasant odour invariably perceived when water-dressing is changed. Here the clean metallic surface presenting no recesses, like those of porous lint, for the septic germs to develop in, the fluid exuding from the surface of the granulations has flowed away undecomposed, and the result is absence of suppuration. This simple experiment illustrates the important fact, that granulations have no inherent tendency to form pus, but do so only when subjected to a preternatural stimulus. Further, it shows that the mere contact of a foreign body does not of itself stimulate granulations to suppurate; whereas the presence of decomposing organic matter does. These truths are even more strikingly exemplified by the fact, which I have elsewhere recorded,* that a piece of dead bone, free from decomposition, may not only fail to induce the granulations around it to suppurate, but may actually be absorbed by them; whereas a bit of dead bone soaked with putrid pus infallibly induces suppuration in its vicinity.

Another instructive experiment is to dress a granulating sore with some of the putty above described, overlapping the sound skin extensively, when we find in the course of twenty-four

* See *The Lancet*, March 23rd, 1867.

hours that pus has been produced by the sore, although the application has been perfectly antiseptic; and, indeed, the larger the amount of carbolic acid in the paste the greater is the quantity of pus formed, provided we avoid such a proportion as would act as a caustic. The carbolic acid, though it prevents decomposition, induces suppuration—obviously by acting as a chemical stimulus; and we may safely infer that putrescent organic materials (which we know to be chemically acrid) operate in the same way.

In so far, then, carbolic acid and decomposing substances are alike—namely, that they induce suppuration by chemical stimulation, as distinguished from what may be termed simple inflammatory suppuration, such as that in which ordinary abscesses originate, where the pus appears to be formed in consequence of an excited action of the nerves, independently of any other stimulus. There is, however, this enormous difference between the effects of carbolic acid and those of decomposition—viz., that carbolic acid stimulates only the surface to which it is first applied, and every drop of discharge that forms weakens the stimulant by diluting it. But decomposition is a self-propagating and self-aggravating poison; and if it occurs at the surface of a severely injured limb, it will spread into all its recesses so far as any extravasated blood or shreds of dead tissue may extend, and, lying in these recesses, it will become from hour to hour more acrid till it acquires the energy of a caustic, sufficient to destroy the vitality of any tissues naturally weak from inferior vascular supply, or weakened by the injury they sustained in the accident.

Hence it is easy to understand how, when a wound is very large, the crust beneath the rag may prove here and there insufficient to protect the raw surface from the stimulating influence of the carbolic acid in the putty, and the result will be, first, the conversion of the tissues so acted on into granulations, and subsequently the formation of more or less pus. This, however, will be merely superficial, and will not interfere with the absorption and organisation of extravasated blood or dead tissues in the interior; but, on the other hand, should decomposi-

tion set in before the internal parts have become securely consolidated, the most disastrous results may ensue.

I left behind me in Glasgow a boy, thirteen years of age, who between three and four weeks previously met with a most severe injury to the left arm, which he got entangled in a machine at a fair. There was a wound six inches long and three inches broad, and the skin was very extensively undermined beyond its limits, while the soft parts generally were so much lacerated that a pair of dressing forceps introduced at the wound, and pushed directly inwards, appeared beneath the skin at the opposite aspect of the limb. From this wound several tags of muscle were hanging, and among them there was one consisting of about three inches of the triceps in almost its entire thickness; while the lower fragment of the bone, which was broken high up, was protruding four and a half inches, stripped of muscle, the skin being tucked in under it. Without the assistance of the antiseptic treatment, I should certainly have thought of nothing else but amputation at the shoulder-joint; but as the radial pulse could be felt, and the fingers had sensation, I did not hesitate to try to save the limb, and adopted the plan of treatment above described, wrapping the arm from the shoulder to below the elbow in the antiseptic application, the whole interior of the wound, together with the protruding bone, having previously been freely treated (p. 355) with strong carbolic acid. About the tenth day the discharge, which up to that time had been only sanious and serous, showed a slight admixture of slimy pus, and this increased till, a few days before I left, it amounted to about three drachms in twenty-four hours. But the boy continued, as he had been after the second day, free from unfavourable symptoms, with pulse, tongue, appetite, and sleep natural, and strength increasing, while the limb remained, as it had been from the first, free from swelling, redness, or pain. I therefore persevered with the antiseptic dressing, and before I left, the discharge was already somewhat less, while the bone was becoming firm. I think it likely that in that boy's case I should have found merely a superficial sore had I taken off all the dressings at the end of three weeks, though, considering the

extent of the injury, I thought it prudent to let the month expire before disturbing the rag next to the skin. But I feel sure that if I had resorted to ordinary dressing when the pus first appeared, the progress of the case would have been exceedingly different.

The next class of cases to which I have applied the antiseptic treatment is that of abscesses. Here, also, the results have been extremely satisfactory, and in beautiful harmony with the pathological principles indicated above. The pyogenic membrane, like the granulations of a sore, which it resembles in nature, forms pus, not from any inherent disposition to do so, but only because it is subjected to some preternatural stimulation. In an ordinary abscess, whether acute or chronic, before it is opened, the stimulus which maintains the suppuration is derived from the presence of the pus pent up within the cavity. When a free opening is made in the ordinary way, this stimulus is got rid of; but the atmosphere gaining access to the contents, the potent stimulus of decomposition comes into operation, and pus is generated in greater abundance than before. But when the evacuation is effected on the antiseptic principle, the pyogenic membrane, freed from the influence of the former stimulus without the substitution of a new one, ceases to suppurate (like the granulations of a sore under metallic dressing), furnishing merely a trifling amount of clear serum, and, whether the opening be dependent or not, rapidly contracts and coalesces. At the same time any constitutional symptoms previously occasioned by the accumulation of the matter are got rid of without the slightest risk of the irritative fever or hectic hitherto so justly dreaded in dealing with large abscesses.

In order that the treatment may be satisfactory, the abscess must be seen before it has opened. Then, except in very rare and peculiar cases,* there are no septic organisms in the contents, so that it is needless to introduce carbolic acid into the

* As an instance of one of these exceptional cases, I may mention that of an abscess in the vicinity of the colon, and afterwards proved by post-mortem examination to have once communicated with it. Here the pus was extremely offensive when evacuated, and exhibited vibrios under the microscope.

interior. Indeed, such a proceeding would be objectionable, as it would stimulate the pyogenic membrane to unnecessary supuration. All that is necessary is to guard against the introduction of living atmospheric germs from without, at the same time that free opportunity is afforded for the escape of discharge from within.

I have so lately given elsewhere* a detailed account of the method by which this is effected, that it is needless for me to enter into it at present, further than to say that the means employed are the same as those described above for the superficial dressing of compound fractures—namely, a piece of rag dipped in the solution of carbolic acid in oil, to serve as an antiseptic curtain, under cover of which the abscess is evacuated by free incision; and the antiseptic paste, to guard against decomposition occurring in the stream of pus that flows out beneath it: the dressing being changed daily till the sinus has closed.

The most remarkable results of this practice in a pathological point of view have been afforded by cases where the formation of pus depended upon disease of bone. Here the abscesses, instead of forming exceptions to the general class in the obstinacy of the suppuration, have resembled the rest in yielding in a few days only a trifling discharge; and frequently the production of pus has ceased from the moment of the evacuation of the original contents. Hence it appears that caries, when no longer labouring, as heretofore, under the irritation of decomposing matter, ceases to be an opprobrium of surgery, and recovers like other inflammatory affections. In the publication before alluded to† I have mentioned the case of a middle-aged man with psoas abscess depending on diseased bone, in whom the sinus finally closed after months of patient perseverance with the antiseptic treatment. Since that article was written, I have had another instance of success, equally gratifying, but differing in the circumstance that the disease and the recovery were both more rapid in their course. The patient was a blacksmith who had suffered four and a half months before I saw him from

* See *The Lancet* of July 27th, 1867.

† *Ibid.*

symptoms of ulceration of cartilage in the left elbow. These had latterly increased in severity, so as to deprive him entirely of his night's rest and of appetite. I found the region of the elbow greatly swollen, and on careful examination discovered a fluctuating point at the outer aspect of the articulation. I opened it on the antiseptic principle, the incision evidently penetrating to the joint, giving exit to a few drachms of pus. The medical gentleman under whose care he was (Dr. Macgregor of Glasgow) supervised the daily dressing with the carbolic-acid paste till the patient went to spend two or three weeks at the coast, when his wife was entrusted with it. Just two months after I opened the abscess he called to show me the limb, stating that the discharge had for at least two weeks been as little as it then was—a trifling moisture upon the paste, such as might be accounted for by the little sore caused by the incision. On applying a probe guarded with an antiseptic rag, I found that the sinus was soundly closed, while the limb was free from swelling or tenderness; and, although he had not attempted to exercise it much, the joint could already be moved through a considerable angle. Here the antiseptic principle had effected the restoration of a joint which on any other known system of treatment must have been excised.

Ordinary contused wounds are of course amenable to the same treatment as compound fractures, which are a complicated variety of them. I will content myself with mentioning a single instance of this class of cases. In April last a volunteer was discharging a rifle, when it burst, and blew back the thumb with its metacarpal bone, so that it could be bent back as on a hinge at the trapezial joint, which had evidently been opened, while all the soft parts between the metacarpal bones of the thumb and forefinger were torn through. I need not insist before my present audience on the ugly character of such an injury. My house-surgeon, Mr. Hector Cameron, applied carbolic acid to the whole raw surface, and completed the dressing as if for compound fracture. The hand remained free from pain, redness, or swelling, and, with the exception of a shallow groove, all the wound consolidated without a drop of matter, so that if it

had been a clean cut, it would have been regarded as a good example of primary union. The small granulating surface soon healed, and at present a linear cicatrix alone tells of the injury he sustained, while his thumb has all its movements and his hand a firm grasp.

If the severest form of contused and lacerated wounds heal thus kindly under the antiseptic treatment, it is obvious that its application to simple incised wounds must be merely a matter of detail. I have devoted a good deal of attention to this class, but I have not as yet pleased myself altogether with any of the methods I have employed. I am, however, prepared to go so far as to say that a solution of carbolic acid in twenty parts of water, while a mild and cleanly application, may be relied on for destroying any septic germs that may fall upon the wound during the performance of an operation; and also that for preventing the subsequent introduction of others, the paste above described, applied as for compound fractures, gives excellent results. Thus I have had a case of strangulated inguinal hernia, in which it was necessary to take away half a pound of thickened omentum, heal without any deep-seated suppuration or any tenderness of the sac or any fever; and amputations, including one immediately below the knee, have remained absolutely free from constitutional symptoms.

Further, I have found that when the antiseptic treatment is efficiently conducted, ligatures may be safely cut short and left to be disposed of by absorption or otherwise. Should this particular branch of the subject yield all that it promises, should it turn out on further trial that when the knot is applied on the antiseptic principle, we may calculate as securely as if it were absent on the occurrence of healing without any deep-seated suppuration; the deligation of main arteries in their continuity will be deprived of the two dangers that now attend it—viz., those of secondary hemorrhage and an unhealthy state of the wound. Further, it seems not unlikely that the present objection to tying an artery in the immediate vicinity of a large branch may be done away with; and that even the innominate, which has lately been the subject of an ingenious experiment by

one of the Dublin surgeons on account of its well-known fatality under the ligature from secondary hemorrhage, may cease to have this unhappy character, when the tissues in the vicinity of the thread, instead of becoming softened through the influence of an irritating decomposing (p. 356) substance, are left at liberty to consolidate firmly near an unoffending though foreign body.

It would carry me far beyond the limited time which, by the rules of the Association, is alone at my disposal, were I to enter into the various applications of the antiseptic principle in the several special departments of surgery.

There is, however, one point more that I cannot but advert to—namely, the influence of this mode of treatment upon the general healthiness of a hospital. Previously to its introduction, the two large wards in which most of my cases of accident and of operation are treated were amongst the unhealthiest in the whole surgical division of the Glasgow Royal Infirmary, in consequence, apparently, of these wards being unfavourably placed with reference to the supply of fresh air; and I have felt ashamed, when recording the results of my practice, to have so often to allude to hospital gangrene or pyaemia. It was interesting, though melancholy, to observe that, whenever all, or nearly all, the beds contained cases with open sores, these grievous complications were pretty sure to show themselves; so that I came to welcome simple fractures, though in themselves of little interest either for myself or the students, because their presence diminished the proportion of open sores among the patients. But since the antiseptic treatment has been brought into full operation, and wounds and abscesses no longer poison the atmosphere with putrid exhalations, my wards, though in other respects under precisely the same circumstances as before, have completely changed their character; so that during the last nine months not a single instance of pyaemia, hospital gangrene, or erysipelas has occurred in them.

As there appears to be no doubt regarding the cause of this change, the importance of the fact can hardly be exaggerated.



On the Effects of the Antiseptic System of Treatment upon the Salubrity of a Surgical Hospital

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THE antiseptic system of treatment has now been in operation sufficiently long to enable us to form a fair estimate of its influence upon the salubrity of an hospital.

Its effects upon the wards lately under my care in the Glasgow Royal Infirmary were in the highest degree beneficial, converting them from some of the most unhealthy in the kingdom into models of healthiness. The interests of the public demand that this striking change should be made generally known; and in order to do justice to the subject, it is necessary, in the first place, to allude shortly to the position and circumstances of the wards.

Each of the four surgeons of the infirmary had charge of three large wards, two male and one female, besides several small ones for special cases. Of these, the most important were the male accident ward and that for female patients, the former containing the chief operation cases as well as those of injury. The third main ward of each surgeon was devoted to chronic male cases, and was in the old infirmary building; but the other two were in the "New Surgical Hospital," erected nine years ago. This

consists of four stories above a basement, each floor containing two large wards communicating with a central staircase, besides several smaller apartments. The wards are spacious and lofty, and in the centre of each are two open fireplaces, in a column which runs straight up to the roof, conveying the chimneys of all the floors, and also collateral ventilating shafts, which are warmed by the chimneys that accompany them, and, communicating with various apertures in the ceilings, form excellent means of carrying off the vitiated atmosphere, while fresh air is amply supplied by numerous windows at both sides, the beds being placed in the intervals between them, at a considerable distance from each other. Except the serious defect that the water-closets in many cases open directly into the wards, the system of construction seemed all that could be desired.

But, to the great disappointment of all concerned, this noble structure proved extremely unhealthy. Pyæmia, erysipelas, and hospital gangrene soon showed themselves, affecting, on the average, most severely those parts of the building nearest to the ground,* including my male accident ward, which was one of those on the ground-floor; while my female ward was on the floor immediately above. For several years I had the opportunity of making an observation of considerable, though melancholy, interest—viz., that in my accident ward, when all or nearly all the beds contained patients with open sores, the diseases which result from hospital atmosphere were sure to be present in an aggravated form; whereas, when a large proportion of the cases had no external wound, the evils in question were greatly mitigated or entirely absent. This appeared striking evidence that the emanations from foul discharges, as distinguished from the mere congregation of several human beings in the same apartment, constitute the great source of mischief in a surgical hospital. Hence I came to regard simple fractures, though almost destitute of professional interest to myself, and of little value for clinical instruction, as the greatest blessings; because, having no external

* Statistics collected by desire of the managers established the fact that the ground-floor wards were, on the average, most liable to pyæmia, whoever might be the surgeon in charge; and that those on the floor immediately above came next in this respect.

wound, they diminished the proportion of contaminating cases. At this period I was engaged in a perpetual contest with the managing body, who, anxious to provide hospital accommodation for the increasing population of Glasgow, for which the infirmary was by no means adequate, were disposed to introduce additional beds beyond those contemplated in the original construction. It is, I believe, fairly attributable to the firmness of my resistance in this matter that, though my patients suffered from the evils alluded to in a way that was sickening and often heart-rending, so as to make me sometimes feel it a questionable privilege to be connected with the institution, yet none of my wards ever assumed the frightful condition which sometimes showed itself in other parts of the building, making it necessary to shut them up entirely for a time. A crisis of this kind occurred rather more than two years ago in the other male accident ward on the ground-floor, separated from mine merely by a passage 12 ft. broad; where the mortality became so excessive as to lead, not only to closing the ward, but to an investigation into the cause of the evil, which was presumed to be some foul drain. An excavation made with this view disclosed a state of things which seemed to explain sufficiently the unhealthiness that had so long remained a mystery. A few inches below the surface of the ground, on a level with the floors of the two lowest male accident wards, with only the basement area, 4 ft. wide, intervening, was found the uppermost tier of a multitude of coffins, which had been placed there at the time of the cholera epidemic of 1849, the corpses having undergone so little change in the interval that the clothes they had on at the time of their hurried burial were plainly distinguishable. The wonder now was, not that these wards upon the ground-floor had been unhealthy, but that they had not been absolutely pestilential. Yet at the very time when this shocking disclosure was being made, I was able to state in an address which I delivered to the meeting of the British Medical Association in Dublin, that during the previous nine months, in which the antiseptic system had been fairly in operation in my wards, not a single case of pyæmia, erysipelas, or hospital gangrene had occurred in them; and this, be it remem-

bered, not only in the presence of conditions likely to be pernicious, but at a time when the unhealthiness of other parts of the same building was attracting the serious and anxious attention of the managers. Supposing it justifiable to institute an experiment on such a subject, it would be hardly possible to devise one more conclusive.

Having discovered this monstrous evil, the managers at once did all in their power to correct it. The extent of the corrupting mass was so great that it seemed out of the question to attempt its removal; but it was freely treated with carbolic acid and with quick lime, and an additional thickness of earth was laid over it; and, further, a high wall at right angles with the end of the building, and reaching up to the level of the first floor, so as necessarily to confine the bad air most prejudicially, was pulled down, and an open iron railing was substituted for it.

There can be no doubt that these measures must have proved salutary. But even if it were admitted that they cured completely the particular evil against which they were directed, it would still have to be confessed that the situation of the surgical hospital has been far from satisfactory. Besides having along one of its sides the place of sepulture above alluded to, one end of the building is conterminous with the old Cathedral churchyard, which is of large size and much used, and in which the system of "pit burial" of paupers has hitherto prevailed. I saw one of the pits some time since, having been requested to report upon it by one of the civic authorities, who is also a manager of the infirmary, and who, having accidentally discovered what was going on, at once took steps to prevent for the future the occurrence of anything so disgraceful. The pit, which was standing open for the reception of the next corpse, emitted a horrid stench on the removal of some loose boards from its mouth. Its walls were formed, on three sides, of coffins piled one upon another in four tiers with the lateral interstices between them filled with human bones, the coffins reaching up to within a few inches of the surface of the ground. This was in a place immediately adjoining the patients' airing ground, and a few yards only from the windows of the surgical wards. And the pit which I inspected

seems to have been only one of many similar receptacles, for one of the Glasgow newspapers contains a statement that "the Dean of Guild is said to have computed that five thousand bodies were lying in pits, holding eighty each, in a state of decomposition, around the Infirmary."^{*} Just beyond the churchyard rises an eminence covered by an extensive necropolis, which, however, from its greater distance, must have comparatively little deleterious influence. When I add that what is called the fever hospital,[†] also a long four-storied building, extends at right angles to the new surgical hospital, separated from it by only eight feet, and that the entire infirmary, containing 584 beds, stands upon an area of two acres, and that the institution is almost always full to overflowing,[‡] I have said enough to show that the wards at my disposal have been sufficiently trying for any system of surgical treatment. Yet, during the two years and a quarter that elapsed between the Dublin meeting and the time of my leaving Glasgow for Edinburgh, those wards continued in the main as healthy as they had been during the previous nine months. Adding these two periods together, we have three years of immunity from the ordinary evils of surgical hospitals, under circumstances which, but for the antiseptic system, were especially calculated to produce them.[§]

It may be well to mention in detail some facts regarding the comparative frequency, before and after the period referred to, of the three diseases to which surgical wards have hitherto

^{*} I doubt if even my sense of the importance of the subject I am dealing with would have induced me to enter into these disagreeable details, were I not able at the same time to bear my testimony to the zealous manner in which the managers of the Infirmary and the Town Council are exerting themselves to correct the evils referred to. I understand that it is in contemplation to abolish entirely intra-mural interment in Glasgow.

[†] About half the wards of the fever hospital are used for surgical cases.

[‡] The rapid increase of Glasgow has rendered the Infirmary, in spite of considerable additions of late years, quite inadequate to the wants of the population; but this evil will shortly be remedied by the construction of a general hospital in connexion with the new College.

[§] The antiseptic system was commenced nearly five years ago, but was for the first two years employed almost exclusively in compound fractures and abscesses, which form but a small proportion of surgical cases, so that the system cannot be said to have been in operation for more than three years with reference to the subject of the present paper.

been peculiarly liable—namely, pyæmia, erysipelas, and hospital gangrene.

And first of pyæmia. This fearful disease used to occur principally in two classes of cases—namely, compound fractures and the major amputations. In compound fracture, it was so rife just before the introduction of the antiseptic system that I had one of the sulphites administered internally as a prophylactic, in accordance with Polli's views, to every patient admitted with this kind of injury; though I cannot say that we observed any distinct evidence of advantage from the practice. But since I began to treat compound fractures on the antiseptic system, while no internal treatment has been used, I have not had pyæmia in a single instance, although I have had in all thirty-two cases—six in the forearm, five in the arm, eighteen in the leg, and three in the thigh. These cases do not include those in which the injury was so great as to demand immediate amputation. But it must be remarked that many of the limbs saved were so severely injured that I should formerly have removed them without hesitation. I almost forget the kind of considerations which used to determine me to amputate under the old treatment; though I know that experience taught us that it was only in comparatively mild cases that it was justifiable to attempt to save the limb. Now, however, there is scarcely any amount or kind of injury of bones, joints, or soft parts which I regard as inconsistent with conservative treatment, except such destruction of tissue as makes gangrene of the limb inevitable as an immediate consequence.

But I may take this opportunity of observing that the attempt to save a limb which, under ordinary treatment, would be subjected to immediate amputation, ought not to be made lightly, or without a thorough acquaintance with some trustworthy method of carrying out the antiseptic system; by which I mean, not the mere use of an antiseptic, however potent, *but such management of the case as shall effectually prevent the occurrence of putrefaction in the part concerned*. Without this such endeavors are far worse than useless; for by the time that local disturbance and constitutional disorder have made it apparent that the antiseptic

means have failed, the patient is so much prostrated by irritation and blood-poisoning, that the operation, if performed, is probably too late; and thus a loose and trifling style of "giving the treatment a trial" swells the death-rate at once of compound fracture and of amputation.

On the other hand, the surgeon will not on this account be justified in contentedly pursuing the old practice of primary amputation; for the antiseptic means which it has been the main labor of the last five years of my life to improve are now so satisfactory* that anyone duly impressed with the importance of the subject, and devoting to it the study and practical attention which it demands, will, with little trouble to himself, securely attain the results which he desires.

I lately visited my wards in Glasgow after an absence of some weeks, and saw, amongst other cases, a compound dislocation of the ankle in a man who had fallen about four feet from the platform at a railway station, and lighted on the outer side of the right foot, which had been forced violently inwards, producing a contused and lacerated wound, about four inches long, crossing the external maleolus, and communicating with the articulation. When I saw the patient the wound had been converted into a superficial sore, cicatrising rapidly; and there had been from first to last no deep-seated suppuration, nor any local or constitutional disturbance. I asked my then house-surgeon, Mr. James Coats, with whom the most critical part of the treatment had rested, whether he could reckon pretty securely upon such results. He replied, "With certainty." I asked the question for the sake of others who were standing by, having little doubt what the answer would be, for when I left him in charge I felt sure that the antiseptic management of the cases would be as satisfactorily conducted as if I were present.

At the same time, it is only right to add, that when he entered upon his office, though convinced of the truth of the theory of the antiseptic treatment, he by no means felt the confidence in

* I hope to bring before the profession the improved antiseptic means above alluded to by publishing from time to time in *The Lancet* cases illustrative of their employment.

carrying it out which he has since acquired; and if an able man like Mr. Coats, imbued with the principles which I have striven to establish, required some practical initiation into the subject before he could be regarded as trustworthy, still more must such be the case with those who, educated in the old system, and long habituated to its practice, have to unlearn cherished ideas and instinctive habits.

But, returning from this digression, I must now speak of pyæmia after the major amputations, before and after the introduction of the antiseptic system.

The hospital records are unfortunately imperfect for one of the three years immediately preceding the antiseptic period. In the other two years, the mortality after amputations in my wards may be gathered from the following tables;—

Before the Antiseptic Period

1864

Seat of Amputation	No. of Amputations	Recoveries	Deaths
Shoulder.....	1	0	1
Arm.....	3	1	2
Forearm.....	3	2	1
Thigh.....	1	1	0
Leg.....	4	3	1
Knee.....	2	1	1
Ankle.....	3	2	1
Totals.....	17	10	7

1866

Arm.....	2	1	1
Elbow.....	1	0	1
Forearm.....	2	2	0
Thigh.....	4	0	4
Knee.....	6	4	2
Leg.....	1	1	0
Ankle.....	2	1	1
Totals.....	18	9	9

On the other hand we have—

During the Antiseptic Period

1867			
Seat of Amputation	No. of Amputations	Recoveries	Deaths
Arm.....	1	1	0
Forearm.....	2	2	0
Knee.....	2	2	0
Leg.....	1	1	0
Ankle.....	1	1	0
Totals.....	7	7	0
1868			
Shoulder.....	1	1	0
Forearm.....	2	2	0
Thigh.....	1	1	0
Knee.....	8	5	3
Ankle.....	5	5	0
Totals.....	17	14	3
1869			
Shoulder.....	2	2	0
Arm.....	2	2	0
Forearm.....	2	1	1
Thigh.....	1	0	1
Knee.....	3	2	1
Leg.....	3	3	0
Ankle.....	3	3	0
Totals.....	16	13	3

Comparing the aggregate results, we have—

Before the antiseptic period, 16 deaths in 35 cases; or 1 death in every 2 1-5 cases.

During the antiseptic period, 6 deaths in 40 cases; or 1 death in every 6 2-3 cases.

These numbers are, no doubt, too small for a satisfactory statistical comparison: but, when the details are considered, they are highly valuable with reference to the question we are considering. This is especially the case with amputation in the upper limb, where neither injuries requiring primary amputation nor the operations involve, as a general rule, much loss of blood or shock to the system; so that, if death does occur, it is

commonly the result of the would assuming unhealthy characters. It happens that there were 12 amputations altogether in the upper limb in each of the two periods referred to. On the 12 cases before the antiseptic period, no fewer than 6 died—a frightful mortality certainly. And it is recorded that, of those 6, 4 died of pyæmia, and 1 of hospital gangrene. Also that one of those which recovered had pyæmia; but, though the symptoms were well marked and severe, presented an example, unhappily too rare, of recovery from the disease.

Very different was the result of corresponding amputations during the antiseptic period. Eleven of the 12 cases recovered; and the one death which did occur was not the result of the operation, but took place in spite of it, from pyæmia, which had resulted from fetid suppuration in a metacarpal bone, and continued after I had removed the hand, in the faint hope that the constitutional mischief might be thrown off when its original source had been taken away. Some of the successful cases, I may add, were by no means favorable subjects for operation: as, for instance, a completely shattered hand in a very aged person; the avulsion by machinery of nearly the entire arm, one of the flaps of the amputation at the shoulder-joint being left contused and lacerated as it had been formed by the injury;* and, again, an enormous osteoid cancer of the upper end of the humerus, involving the deltoid muscle, and permitting only the formation of skin flaps, attended with profuse hæmorrhage, in a patient already anæmic from the disease.

In the lower limb, 28 amputations in all were performed during the antiseptic period. Out of these, death took place in 5; but was generally sufficiently accounted for by the severity of the case, as when the thigh was amputated immediately below the hip-joint in a patient greatly exhausted by hæmorrhage from malignant disease; or, to take another example, when primary amputation was performed at the knee on one side, and immediately below it on the other, in a man who had sustained very severe injuries to both legs, and had been transported a considerable distance by railway to Glasgow.

* This case was treated by my colleague, Dr. Dunlop, during my temporary absence.

In one case only did pyæmia result from the operation—viz., after amputation at the knee in a young man of weakly constitution, where putrefaction occurred in the stump through mismanagement. Here the symptoms of pyæmia presented themselves during life, and the femoral vein was found loaded with pus on dissection. When putrefaction occurs after such an operation, there is no security against pyæmia, even in private practice; and a single instance of the kind in three years, and that in a feeble subject, is certainly no evidence of any peculiarity in the hospital atmosphere.

In mentioning the fact that putrefaction occurred from mismanagement, I do not wish to be understood as implying that it can always be avoided in stumps. In the present state of surgical practice, this is far from being the case. When sinuses exist in connexion with a diseased joint, putrefaction is present in them at the outset; and even if they are injected with an antiseptic solution before the operation, it can never be certain that the liquid penetrates to every recess of these often complicated passages, or destroys the vitality of the putrefactive organisms, lurking, perhaps, in portions of lymph or slough. And if a single such organism remain alive, it will propagate and spread in the wound as soon as the antiseptic applied at the time of the operation has been absorbed into the circulation; and any external antiseptic dressing will, under such circumstances, be of course entirely nugatory. It is, I suspect, for want of bearing this point in mind that disappointment has often been experienced in applying antiseptic treatment to amputations and excisions. The full possible benefits of the system can never be obtained in such cases till it shall be deeply impressed upon the profession and the public that abscesses, more especially those in connexion with diseased joints, must never either be allowed to break of themselves, or be opened without antiseptic precautions.*

* The practice which I have found to answer best in amputations and excisions in parts affected with sinuses is, after injecting the sinuses with a powerful antiseptic, to apply to the cut surface a pretty strong solution of chloride of zinc (say forty grains to an ounce of water), such as was recommended by Mr. Campbell De Morgan, and then employ an external antiseptic dressing, in the hope, though never in the certainty, that putrefaction

I am bound to add that there is another respect in which the antiseptic principle has not yet had justice done to it in the larger amputations in the lower limb. Of all incised wounds, these have proved the most difficult to manage; and putrefaction has repeatedly occurred in my practice, even where no sinuses were present. It was so in the two cases above referred to, of amputation just below the hip-joint for malignant disease, and double primary amputation for injury. Considering the condition of those patients on the day after the operation, I believe both would have recovered had we succeeded in avoiding putrefaction, which, apart altogether from the risk of pyæmia, terribly aggravates formidable cases, like those, by the irritation and prostration which it occasions. Hence we may fairly look for better results in the future from amputation in the lower limb. For I am satisfied that the difficulties of the antiseptic management are not insuperable. I have devoted much attention to this branch of the subject during the last twelve months, and steady progress has been made in it; so that the proportion of stumps in which healing has taken place without any deep-seated suppuration has been markedly increasing, and I anticipate that before long we shall be able to reckon with certainty on the absence of putrefaction in all cases where sinuses are not present.

But to return to the subject of pyæmia. The two cases above alluded to were the only instances of its occurrence in my department during the antiseptic period. One of them requires further notice here. It belonged to a class of injuries in which the benefits of the antiseptic system have been conspicuously apparent—namely, severe contused wounds of the hand or foot, such as are very frequent in a great centre of manufacture like Glasgow. Formerly there were no injuries more unsatisfactory to deal with. The uncertainty of the extent of the damage inflicted by the contusion made it a most perplexing question

will be avoided. Chloride of zinc, having the peculiarity of producing a remarkably persistent antiseptic effect upon the cut surface, protects it during the dangerous period preceding granulation, when the recently divided tissues are both sensitive and prone to absorption; so that even if putrefaction does occur, the risk of inflammation and pyæmia is greatly diminished.

where amputation should be performed. On the one hand, if too little was removed, sloughing of the flaps ensued, or diffuse suppurative inflammation of the weakened tissues infiltrated with extravasated blood; and, on the other hand, if it was determined to avoid that error and to amputate through perfectly sound tissues, an extravagantly large portion of the limb was often sacrificed. It is therefore an unspeakable satisfaction to be able to avoid amputation altogether in such cases, merely taking away such portions as may be actually destroyed, and leaving the weakened tissues in the vicinity to recover themselves quietly, instead of perishing under the irritating and poisoning influence of putrefaction; while any dead portions that may remain are absorbed more or less completely, like the extravasated blood, and replaced by tissue of new formation. If the history of all the contused wounds of the hands and feet that have been treated in my wards during the last three years were recorded, including many compound fractures not reckoned as such in our classification and several compound dislocations, it would be enough to convince the most sceptical of the advantages of the antiseptic system.

But the case to which I am now alluding was an exception to the general rule of satisfactory progress. It was a severe injury to the hand from machinery. My then house-surgeon, who had only just entered upon his office, and had not as yet the confidence in the antiseptic system which he soon afterwards acquired, took it for granted that I should amputate the hand, and committed the error of leaving it till my visit on the following day, without adopting efficient antiseptic measures. When I saw the case I decided to try to save the greater part of the hand, and endeavored to correct the mistake which had been made. Putrefaction, however, ensued, and after some days pyæmia occurred, and continued, as before stated, in spite of amputation of the hand. On dissecting the parts, one of the metacarpal bones was found split up, with putrefactive suppuration developed in its interior. Under such circumstances pyæmia might occur in a perfectly sound constitution and in the most healthy atmosphere, just as, in Cruveilhier's highly instructive experiment,

suppurative phlebitis of the femoral vein and its branches, exactly corresponding to that which is seen in traumatic pyæmia, was induced in a healthy dog by introducing into the vessel a bit of wood which, from its porous nature, could not but originate putrefaction.*

Considering, then, the circumstances of the only two cases of pyæmia which have occurred in my department during the three years of the antiseptic period, I am justified in saying that the wards have been completely freed from their former liability to this frightful scourge.

Next of erysipelas, a disease which, though not so fatal as pyæmia, used not unfrequently to occasion death amongst my patients. During the antiseptic period several cases have been admitted into my wards from without, but one only has originated in them. This occurred in a young man with disease of the foot, accompanied by sinuses extending into the leg. I performed amputation at the ankle, but putrefaction continued in the sinuses; and after the lapse of a considerable period erysipelas occurred in connexion with them. He recovered from the complaint, and after a while went to his lodgings for change of air, with the sinuses still unhealed, and subsequently had another attack of erysipelas there implying that the tendency to it was in his own system rather than in the locality. That such was really the case was afterwards fully demonstrated. The sinuses refusing to heal, and disease recurring in the bones, he was re-admitted under my care, and I performed amputation in the leg above the sinuses. The stump healed without any deep-seated suppuration, presenting a very good example of the result of a modification of Mr. Teale's method of amputation; and I requested him to ascertain, by Mr. Teale's plan of introducing circular pieces of flannel into the socket of the artificial limb, how much of his weight he could conveniently rest upon the end of the stump. As he did not call to report the result on the day arranged, I inquired into the cause, and learned that the stump

* See Cruveilhier's *Anatomie Pathologique*, livraison xi., where will also be found the records of important experiments, proving how readily liquids introduced into the interior of bones pass into the general circulation.

had been seized with a third attack of erysipelas, although perfectly cicatrised without sinus or sore of any kind.* Thus, as regards erysipelas, our only exception to perfect immunity from the disease during the three years was one that strikingly proves the rule.

It remains to speak of hospital gangrene. This was formerly both frequent and severe amongst my patients. It often grievously marred the most promising results of surgery, and sometimes committed fearful ravages. Thus, I have known a boy admitted with a small superficial wound near the elbow, in which hospital gangrene occurring caused such destruction of tissue, deeply as well as superficially, in spite of the most energetic treatment, that it became necessary to amputate the limb. Now and then it led to a fatal result, as in one of the amputations before referred to. In that case I removed the arm at the shoulder-joint for injury in a boy, and for some time all went on well, till I regarded him as perfectly safe; but hospital gangrene came on in the stump, and, advancing insidiously in all directions, defied my best attempts to check it, and had reached beyond the sternum before the poor fellow sank exhausted from its effects.

The contrast under the antiseptic system has been most striking. For the first nine months, as before mentioned, we had not a single case of the disease. Since that time it has shown itself now and then, but in a mild form, invariably yielding to treatment, never occurring in recent cases, but only in old sores weakened by the influence of surrounding cicatrix. But even this has been very rare, and I do not recollect more than one example of it during the last year. In short, hospital gangrene, like pyæmia and erysipelas, may be said to have been banished by the antiseptic system.

Such being the case, I have insensibly relaxed in different ways my former vigilance regarding the wards. I have allowed cribs for children to be introduced without remonstrance, having practically the effect of increasing the number of beds for adults; and I have, in the pressure of deficient accommodation, often

* This case seems to me to possess considerable interest, as something intermediate—as it were a connecting link—between traumatic and idiopathic erysipelas.

permitted two children to be put in one bed—a thing which I should formerly not have thought of. I used to make a point of having both the large fires in each ward kept alight night and day during the heat of summer, for the sake of making the ventilation as perfect as possible. But during the last season the nurses were left to follow their inclination, and keep only one of the fires lighted. I may add that my wards have remained during the three years without the annual cleaning, which used to be thought essential. On my asking the superintendent the reason for the omission, he replied that, as those wards had continued healthy, and there was nothing dirty in their appearance, it had seemed unnecessary to disturb them. Thus the wards have been in various respects subjected to greater trial than usual, and yet have remained, as I may repeat without any exaggeration, models of healthiness.

That such should have been the case under the unfavorable hygienic conditions above referred to seems at first sight very surprising. The immediate vicinity of a burying-ground such as has been described, together with the position of the wards at the base of an hospital of four stories, with the air confined by neighboring buildings, may seem conditions utterly inconsistent with health in the patients. That these circumstances were very unfavorable is undoubtedly true; and that they were highly injurious before the antiseptic period seems clearly indicated by our experience. But a little consideration will show that it is not unreasonable to suppose them of secondary importance—as aggravators of the evil, rather than the essential causes of it. The corpses in the places of sepulture beside the infirmary were for the most part covered by at least some inches of earth, which has a most powerful effect in checking the evolution of noxious effluvia; and even the foul gases from the open pits were perpetually diluted by the air with which they mingled, so that but a small proportion of them would enter the wards; and accordingly, when the patients were cleared out for the purpose of the annual cleaning, there was nothing in the wards to offend the nose. But the emanations from sores are poured directly into the confined atmosphere in which the patients are: and anyone familiar with

the faint sickly smell commonly perceptible in surgical wards under ordinary treatment, and still more with the stench which prevails at the time of the daily dressing, will readily understand that putrid exhalations from the patients may be a source of mischief, compared with which the other circumstances alluded to may be of comparatively trifling consequence.

With the object of getting rid of this great evil as much as possible, I have used antiseptic means, not only where they are of essential importance for the treatment of the individual case concerned, as in recent wounds and abscesses, but also in superficial sores. For though granulating surfaces will commonly heal well enough under a putrid dressing (for such the cleanly water dressing becomes within a few hours of its application), every case so treated furnishes its quota to the vitiation of the general atmosphere of the ward. Hence, for the sake of the inmates generally, it is obviously desirable that healing sores should be dressed with some application which, while permitting, or, if possible, favoring, cicatrisation, should prevent odor. For this purpose some dressing, unstimulating, but at the same time persistent in antiseptic action, is requisite,—a combination which I have sought in various different forms to obtain, and, of late more especially, with very satisfactory results, so that while the healing of superficial sores proceeded with greater rapidity than under water dressing, all my sixty patients might sometimes be dressed without the odor of putrefaction being perceptible in one of them.

The result of this great change has been such as to demonstrate conclusively that the exhalations from foul discharges are the essential source of the insalubrity of surgical wards; and that when this is effectually suppressed, other conditions, which we are accustomed to regard as most pernicious, become powerless to produce serious evil.

It is obvious that the facts recorded in this paper are of extreme importance with reference to the vexed question of hospital construction. With the view of assimilating the atmospheric condition of our large hospitals to that of a private dwelling, it has been lately proposed to do away with them altogether in their

present form, and to substitute for them congeries of cast iron cottages, capable of being occasionally taken down, cleansed, and reconstructed,—a plan which, besides involving enormous expense, would interfere most seriously with efficient supervision of the patients, and with the teaching of students at the bedside. But from what has been related above, it is plain that no material alteration of the existing system will be required. We have seen that a degree of salubrity equal to that of the best private houses has been attained in peculiarly unhealthy wards of a very large hospital, by simply enforcing strict attention to the antiseptic principle. And, considering the circumstances of those wards, it seems hardly too much to expect that the same beneficent change which passed over them will take place in all surgical hospitals, when the principle shall be similarly recognised and acted on by the profession generally. The antiseptic system is continually attracting more and more attention in various parts of the world; and, whether in the form which it has now reached, or in some other and more perfect shape, its universal adoption can be only a question of time. The noble institutions of which our country is justly proud, admirably adapted alike for the treatment of the sick and the instruction of the student, will then be cleared of the only blot that now attaches to them,—the malignant influence of impure atmosphere.

Edinburgh, December, 1869.

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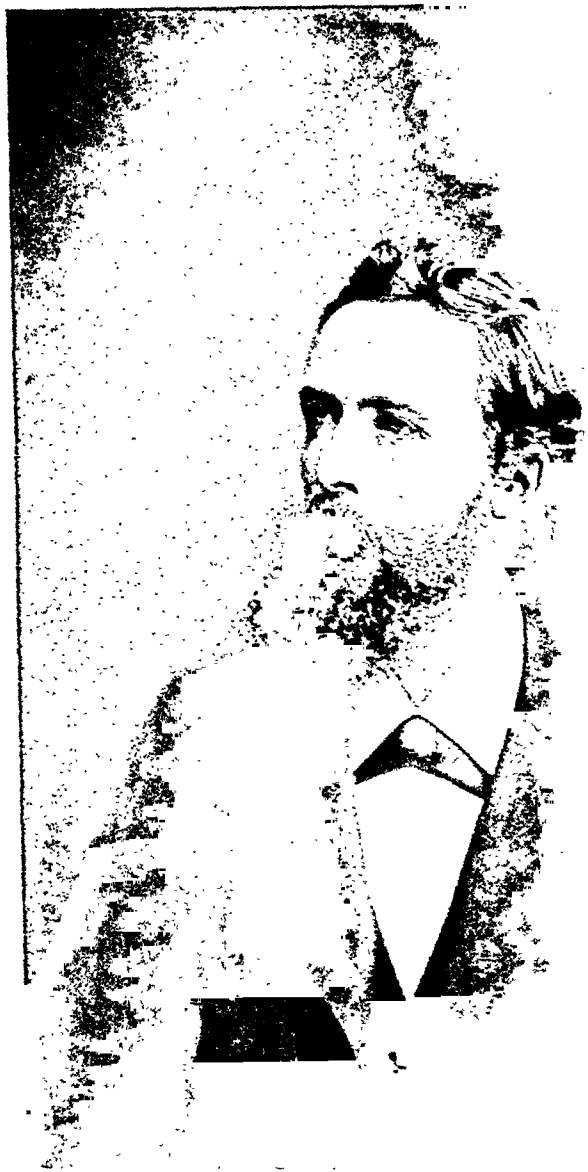
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JOHANN VON MIKULICZ-RADECKI

(In 1878)

From Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie. Dritter Supplementband. Gedenkband für J. von Mikulicz. Jena, G. Fischer, 1907

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Johann Von Mikulicz-Radecki

Austrian Surgeon, 1850-1905

BIOGRAPHY

- 1850 Born May 16, in Cernowicz, in Bukowina, then a part of Austria, now Rumania. Educated at Herrmannstadt. Earned his way through the University by giving lessons on the piano and playing on the organ from 5 to 8 A. M.
- 1875 Age 25. Degree of Doctor of Medicine at Vienna. Became assistant to Billroth.
- 1879 Age 29. Visited Lister in England and Volkmann in Germany.
- 1880 Age 30. Qualified as Privat-docent in surgery in Vienna.
- 1882 Age 32. Became director and Professor of Surgery at Krakow, lectured in Polish.
- 1886 Age 36. First treated cancer of esophagus by resection and plastic transplantation and introduced lateral pharyngotomy in excising malignant tumors of tonsillar region (Garrison).
- 1887 Age 37. Became director of the Clinic and Professor of Surgery at Königsburg.
- 1888 Age 38. First described condition we now call Mikulicz's disease, published in detail in 1892.
- 1890 Age 40. Became Professor of Surgery at Breslau, held position until his death.
- 1902 Age 52. Described in detail the two stage resection of tumors of intestine.
- 1905 Age 55. Died on June 14, following an operation for malignancy of the stomach.

Had 8 children, 4 sons and 4 daughters. Only surviving son (1930) is Prof. Dr. Felix Von Mikulicz-Radecki of the University Frauenklinik of Berlin.

Mikulicz was an accomplished musician and was a friend of Brahms.

EPONYMS

CELLS: "Foam cells," the cells in rhinoscleroma which contain the bacilli of the disease (*Bacillus rhinoscleromatis*). See bibliographic reference No. 1, 1876.

DICTUM: It is highly dangerous to give a general anesthetic to a patient whose hemoglobin is below 30. See bibliographic reference No. 65, 1890.

DISEASE: Chronic, hypertrophic enlargement of lacrymal and salivary glands. See bibliographic reference No. 71, 1892 and complete, original article with English translation in this monograph.

DRAIN: For large cavities where wicks are to be removed gradually; a square of gauze with silk cord in its center is placed into cavity and packed with gauze wicks. See bibliographic reference No. 14, 1881.

KENTROTRIBE: An instrument to crush an intestinal spur in artificial anus, pressure being obtained by an elastic band around the handles, giving a more gradual pressure than with a screw. Illustrated in *Handb. d. prakt. Chir.*, 1903, 2 Aufl., Vol. III, p. 193.

LINE: Also called Mikulicz-Hartmann line, on stomach, used as position for clamp in gastric resection. Line extends from right of midline on greater curvature, nearly to cardia on lesser curvature, allowing excision of pylorus, whole of lesser curvature nearly up to esophagus, corresponding half of greater curvature, right half of great omentum, whole of lesser omentum, glands and lymphatics in the neighborhood of the celiac axis artery, all in one piece. Illustrated in *ibid.*, Vol. IV, p. 173.

MASK: A frame covered with gauze and worn over the mouth and nose of the operating surgeon.

OINTMENT: For atonic granulation tissue, consisting of Balsum of Peru 10 parts, silver nitrate 1 part, petrolatum 100 parts.

OPERATION: Foot, osteoplastic resection of; also called Wladimiroff-Mikulicz operation, consisting of excision of astragalus and calcaneus with apposition of cut ends of cuboid and scaphoid to cut ends of tibia and fibula, weight of body then resting on distal ends of metatarsal bones. See bibliographic reference No. 15, 1881.

OPERATION: Gastroenterostomy, also called Mikulicz-Czerny operation; by using a transverse incision in jejunum three or four inches from its origin and an incision close to the greater curvature of the stomach, a suture anastomosis allows the stomach to drain at the lowest point without possibility of kinking the intestine. See bibliographic reference No. 99, 1897 and *Handb. d. prakt. Chir.*, 1903, Vol. III, p. 175.

OPERATION: Hip, reduction of congenital dislocation, by means of extension. See bibliographic reference No. 86, 1894.

OPERATION: Intestines, resection of, by two stage or exteriorization method; also called Mikulicz-Bruns method of colectomy. See bibliographic reference No. 124, 1902 and complete, original article with English translation in this monograph.

OPERATION: Nasal lobule, shortening of elongated, by partial excision. See bibliographic reference No. 32, 1883.

OPERATION: Pharyngotomy, for exposure of tonsillar tumors. See bibliographic reference No. 37, 1884.

OPERATION: Pyloroplasty, also called Heinecke-Mikulicz operation; a longitudinal incision at pylorus is sutured transversely so that caliber is increased. See bibliographic reference No. 57, 1887.

OPERATION: Rectum, prolapse of; transverse incision through all layers of rectum into peritoneal cavity, excision of prolapsed segment and reunion of ends. See bibliographic reference No. 29, 1883.

OPERATION: Tarsectomy; see osteoplastic resection of foot.

OPERATION: Torticollis, excision of sternomastoid muscle. See bibliographic reference No. 87, 1895.

BIBLIOGRAPHY OF WRITINGS

A—Army Medical Library.

B—New York State Library.

C—New York Academy of Medicine Library.

D—Kings County Medical Society, Brooklyn, Library.

E—Lane Medical Library of Stanford University.

1. Über das Rhinosklerom (Hebra). (On rhinoscleroma (Hebra).) Arch. f. klin. Chir., 20: 485, 1876.
2. Beitrag zur Genese der Dermoide am Kopfe. (Contribution to the origin of dermoids of the head.) Wien. med. Wochensch., 1876.
3. Über individ Formdifferenzen am Femur und an der Tibia des Menschen, mit Berücksichtigung der Statik des Kniegelenks. (On the individual differences in form of the human femur and tibia, with regard to the equilibrium of the knee joint.) Archiv. Anat. Physiol. (Anatom. abthg.), pp. 351-404, 1878. Also: Arch. f. klin. Chir., 23, 1879.
4. Über die Beziehungen des Glyzerius zur Coccobacteria septica und zur septischen Infektion. (Relation of glycerine to the septic cocci and to septic infection.) Ibid., 22, 1878. Also: 75 pp., 8°, Berlin, 1878, in A.
5. Die seitlichen Verkrümmungen am Knie und deren Heilungsmethoden. (Genu varum of the knee and its method of cure.) Arch. f. klin. Chir., 23: 561-629; 671-770, 881-884, 1879. Also rep.: Wien. med. Presse, 20: 117-119, 1879.
6. Subperiostale Exstirpation der ganzen Scapula. Vollständige Regeneration. (Subperiosteal removal of the entire scapula. Complete regeneration.) Arch. f. klin. Chir., 24, 1879.
7. Die antiseptische Wundbehandlung und ihre Technik. (Antiseptic wound treatment and its technique.) Mitteil. d. Ver. d. Aerzte in Nieder-Oesterreich, 5: 58; 77; 92-95; 122-124; 146; 161; 183-187, 1879.

8. Exstirpation solider Geschwülste des Uterus und der Ligamenta Lata durch die Laparotomie. (Extirpation of solid tumors of the uterus and of the lateral ligaments by laparotomy.) Wien. med. Wochensch., 29: 513; 544; 576; 599-602, 1879.
9. Über eine Methode zur Aufrichtung eingesunkener Nasen. (A method of restoring a sunken nose.) Ibid., 1201-1206. Also: Anz. a. k. k. Gesellsch. d. Aerzte in Wien, pp. 19-21, 1879.
10. Über Totalexstirpation des Uterus. (Panhysterectomy.) Wien. med. Wochensch., 30: 1281; 1309; 1419; 1880; 31: 9; 37; 93; 150; 184; 215; 241-245, 1881.
11. Zur Sprayfrage. (The question of sprays.) Arch. f. klin. Chir., 25: 707-751; 1880. Also: 45 pp., 8°, Berlin, Schumacher, 1880, in A.
12. Osteomyelitis und Periostitis der rechten Scapula. (Osteomyelitis and periostitis of the right scapula.) Wien. med. Presse, 1880, in A.
13. Bericht über einen Fall von Kompression der Trachea durch ein Aortenaneurysma. (Report of a case of compression of the trachea by an aortic aneurism.) With Zemann. Ibid., 1404. Also: Anz. d. Ges. d. Aerzte in Wien, 1881.
14. Über die Anwendung der Antisepsis bei Laparotomien, mit besonderer Rücksicht auf die Drainage der Peritonealhöhle. (Use of antisepsis in laparotomies, with special regard to drainage of the peritoneal cavity.) Arch. f. klin. Chir., 26: 111-150, 1881.
15. Eine neue osteoplastische Resektionsmethode am Fusse. (A new method of osteoplastic resection of the foot.) Ibid., 494-501. Also: Langen's Arch., Bd. 26, Hft. 2. Also: Chirurgenkongress, 1881. Also: 8 pp., 1 pl., 8°, Berlin, Schumacher, 1881, in A & C.
16. Demonstration eines geheilten Falles von osteoplastischer Resektion des Fusses nach seiner Methode. (Demonstration of a cured case of osteoplastic resection of the foot by his (Mikulicz) method.) Prag. med. Wochensch., 6: 236, 1881.

17. Demonstration des Leiterscher Wärmeregulators. (Demonstration of Leiter's Heat-regulator.) Chirurgenkongress, 1881.
18. Zur Nervesdehung bei Erkrankungen des Rückenmarks. (On nerve stretching in diseases of the spine.) With N. Weiss. Wien. med. Wochensch., 31: 1013; 1045; 1069; 1149; 1200; 1258; 1312; 1397; 1477; 32: 96; 188; 357, 1881. Also: Mitth. d. Wien. med. Doct.-Coll., 8: 177-122, 1882.
19. Über Gastroskopie und Oesophagoskopie. (On gastroscopy and esophagoscopy.) Wien. med. Presse, 22: 1405-1408; 1437; 1473; 1505; 1537; 1573; 1629, 1881. Also: Allg. Wien. med. Zeitg., 26: 456, 1881. Also: Wien. med. Bl., 4: 1362-1364, 1881. Also: Zentralbl. f. Chir., 8: 673-676, 1881. Also: Anz. d. k. k. Gesellsch. d. Aerzte in Wien, pp. 15-18, 1881. Also: 32 pp., 8°, Wien., Urban, 1881, in A. Also: Chirurgenkongress, 1882. Also: Mitth. d. Ver. d. Aerzte in Nied.-Oest., Wien, 8: 23-28, 1882.
20. Beiträge zur Kenntniss und chirurgischen Behandlung der puerperalen Pyohemie mit Einschluss einiger progredienter nicht metastatischer Entzündungsprocesse im Puerperium. (Contribution to the knowledge and surgical treatment of puerperal pyemia including some extending but not metastatic processes in the puerperium.) With A. Felsenreich. Zeitsch. f. Heilk., 2: 112-153, 1881.
21. Demonstration an der Leiche der Pylorusresektion. (Demonstration on the cadaver of pyloric resection.) Demonstration der von Billroth bisher resezierten Pylorusstücke. (Demonstration of Billroth's resection of a portion of the pylorus.) Chirurgenkongress, 1881.
22. Über die Verwendung des Jodoforms bei der Wundbehandlung und dessen Einfluss auf fungöse und verwandte Prozesse. (Application of iodoform in wound treatment and its influence on fungoid and related processes.) Chirurgenkongress, 1881. Also: Wien. med. Presse, 22: 734-737, 1881. Also: Wien. med. Wochensch., 31: 649-651, 1881. Also: in Polish, O zyciu jodoformu w leczeniu

tan. Przegl. lek., Karkow, 20: 481; 493; 505; 519; 534; 547; 564; 577; 593, 1881. Also: Arch. f. klin. Chir., 27: 196-239, 1882.

23. Weitere Erfahrungen über die Verwendung des Jodoforms in der Chirurgie. (Further experiences in the use of iodoform in surgery.) Berl. klin. Wochensch., 18: 721; 741, 1881. Also: Mitth. d. Wien. med. Doct.-Coll., 7: 413-419, 1881. Also: 23 pp., 8°, Berlin, Schumacher, 1881, in A. Also: Wien. Klinik, 8: 1-39, 1882. Also: English translation in The Best Surgical Dressing, by O. K. Newell, pp. 15-119, 1888. Also: Berliner klin. Wochensch., 19: 62, 1882. Also: Centralbl. f. Chir. 9: 1, 1882.
24. Die Bedeutung der modernen Chirurgie für den klinischen Unterricht. (The significance of modern surgery on clinical instruction.) Wien. med. Wochensch., 32: 1415-1420, 1882. Also: in Polish, O wpływie chirurgii nowoczesnejma kształcenie uczniów w klinice chirurgicznej. Przegląd lekarsk., Krakow, 21: 569-572, 1882.
25. Przyczyunki do chirurgii. (Introductory lecture to surgery.) Przegl. lek., Krakow, 22: 1; 17, 1883.
26. Über einen geheilten Fall von günstig verlaufener Pylorusresektion, nebst Bemerkungen über ein gastroskopisches Symptom des Magenkarzinoms. (A case of resection of the pylorus with favorable progress to recovery together with remarks on a gastroscopic symptom of gastric carcinomas.) Chirurgenkongress, 1883. Also: Centralbl. f. Chir., 1883. Also: Wien. med. Wochensch., 33: 705; 745, 1883. Also: Przegl. lek., Krakow, 22: 157; 169, 1883.
27. Zweikindskopfgrosses interstitielles und orangegrosses subseröses Myofibrom des Uterus. Exstirpation durch die Scheide; Heilung. (Interstitial myofibroma of the uterus twice as large as a child's head and a subserous one as large as an orange. Extirpation through the vagina; recovery.) Wien. med. Wochensch., 33: 269-273, 1883. Also: Przegl. lek., Krakow, 22: 17; 29, 1883.

28. Skoliosometer, ein Apparat zur Messung der Skoliose. (Scoliosometer, an apparatus for measurement of scoliosis.) Chirurgenkongress, 1883. Also: Centralbl. f. Chir., 10: 305-311, 1883. Also: Przegl. lek., Krakow, 22: 141-143, 1883.
29. Invagination und Prolaps des Dickdarms durch den Mastdarm; Resektion eines 76 cm. langen Darmstückes; Heilung. (Intussusception and prolapse of large intestine through the rectum; resection of 76 cm. of intestine; recovery.) Wien. med. Press, 50: 1565; 51: 1597-1602, 1883. Also: Gazeta lekarska, Warszawa, 2. s., 3: 901-903, 1883.
30. Zur Gussenbauerschen Operationsmethode bei fibrösen Nasenrachenpolypen. (The operation of Gussenbauer for fibrous naso-pharyngeal polypi.) Prag. med. Wochensch., 8: 409; 417, 1883. Also: Przegl. lek., Krakow, 22: 53-55, 1883.
31. Zwei Fälle von osteoplastischer Fussresektion nach eigener Methode. (Two cases of osteoplastic resection of the foot by his particular method.) Report in Wien. med. Wochensch., 33: 1485-1490, 1883. Also: Przegl. lek., Krakow, 22: 441; 455, 1883.
32. Przyczynki do plastycznej chirurgii nosa. (Contribution to plastic surgery of the nose.) Gazeta lekarska, Warszawa, 2. s., 3: 429; 453, 1883. Also: Arch. f. klin. Chir., 30: 106-118, 1884.
33. Erste Hilfe für Verwundete. (First aid for wounded.) Org. d. milit.-wissenschaftl. Ver., 27, 1883.
34. Przyczynek do techniki operacyjnej in nastopomego leczenia raka migdalkow. (Operation in gangrene of tonsils and after-treatment.) Przegl. lek., Krakow, 22: 597; 609, 1883.
35. Über die Bedeutung der Bluttransfusion und Kochsalzinfusion bei akuter Anämie. (The importance of blood transfusion and common salt infusion in acute anemia.) Wien. Klin., 10: 181-199, 1884.
36. O dzisiejszym stanie nauki o transfuzji. (The present

state of knowledge respecting transfusion.) *Prezgl. lek.*, Krakow, 23: 177; 189; 201, 1884.

37. Zur Operation des Tonsillarkarzinoms; ein Beitrag zur Pharyngotomie. (The operation for carcinoma of tonsil; a contribution to pharyngotomy.) *Deutsch. med. Wochensch.*, 10: 33-35, 1884.
38. Über Laparotomie bei Magen- und Darmperforation. (Laparotomy for perforation of stomach and intestine.) *Naturf.-Versamml. Magdeburg*, 1884. Also: *Volkmann's Samml. klin. Vortr.*, No. 262, *Chir.*, No. 83: 2307-2334, 1885. Also: *Przegl. lek.*, Krakow, 24: 89; 105; 165; 179; 208, 1885.
39. Beiträge zur Wundbehandlung. (Contributions to wound treatment.) *Wien. med. Wochensch.*, 34: 1045; 1069; 1099; 1153; 1181; 1212; 1273; 1357; 1396, 1884. Also: *Przegl. lek.*, Krakow, 23: 1; 55; 70; 393; 411; 421; 433; 445; 553; 565, 1884.
40. Über den Wert des Jodoforms für Wunden in Schleimhauthöhlen. (Value of iodoform for wounds in cavities of mucous membrane.) *Wien. med. Presse*, 25: 1154, 1884. Also: *Inter. med. Kongr.*, Kopenhagen, 1884, 8: 114-121, 1885.
41. Antiseptik bei der Laparotomie. (Antisepsis in laparotomy.) *Ibid.*, 1884, pp., 40-44, 1886.
42. Über einige Modifikationen des antiseptischen Verfahrens. (Modifications of antiseptic treatments.) *Chirurgenkongress*, pp. 8-14, 1884. Also: *Centralbl. f. Chir.*, 1884. Also: *Arch. f. klin. Chir.*, 31: 435-488, 1885.
43. Zur Blutstillung durch Tamponade und Kompression. (The arrest of hemorrhage by tamponade and compression.) *Chirurgenkongress*, pp. 31-33, 1884. Also: *Centralbl. f. Chir.*, 1884. Also: *Arch. f. klin. Chir.*, 31: 489-493, 1885.
44. Über die Resektion des Kropfes, nebst Bemerkungen über die Folgezustände der Totalexstirpation der Schilddrüse. (Resection of goiter, with remarks on the results of total removal of the thyroid.) *Centralbl. f. Chir.*, 1885.

45. O resekcyi wola wraz z wagami o następstwach całkowitego wyluszczenia gruczoła tarczowego. (Paralysis of the muscles of the larynx shortly after extirpation of goiter.) Przegl. lek., Krakow, 24: 609, 1885.
46. O tradzie. Über den Aussatz. (Tragedy. Concerning leprosy.) Ibid.
47. Przyczynek do operacyi wola ze szczegolnem uwzględnieniem złych następstw. (Extirpation of goiter with singularly complicated sequelae.) Gazeta lek., Warszawa, 2. s., 6: 5; 26, 1886.
48. Beitrag zur Operation des Kropfes. (Contribution to the operation for goiter.) Wien. med. Wochensch., 36: 1; 40; 70; 97, 1886.
49. Ein Fall von Resektion des karzinomatösen Oesophagus mit plastischen Ersatz des erzierten Stückes. (Case of resection of carcinomatous esophagus with plastic substitution of the elevated portion.) Prag. med. Wochensch., 11: 93, 1886. Also: 5 pp., 8°, Prag., 1886, in A.
50. Zur Prioritätsfrage der osteoplastischen Resektion am Fusse. (Question of priority in osteoplastic resection of the foot.) Arch. f. klin. Chir., 23, 1886. Also: Przegl. lek., Krakow, 25: 109-111, 1886.
51. Über die Ausschaltung toter Räume aus der Peritonealhöhle, mit besonderer Rücksicht auf die Exstirpation der aus der Beckenhöhle ausgehenden Geschwülste. (Closing off of dead space from the peritoneal cavity with special regard to the extirpation of tumors arising in the pelvic cavity.) Chirurgenkongress, Pt. 2, pp. 187-209, 1886. Also: Centralbl. f. Chir., 24, 1886. Also: Arch. f. klin. Chir., 24: 635-657, 1887.
52. Die seitliche Pharyngotomie behufs Exstirpation maligner Geschwülste der Tonsillargegend. (Lateral pharyngotomy for extirpation of malignant swellings of the tonsillar region.) Deutsch. med. Wochensch., 12: 157; 178, 1886. Also: Przegl. lek., Krakow, 25: 173, 1886; 26: 351, 1887.

53. Przyczynki do chirurgii jamy brzusznej. (Contributions to surgery of abdomen.) Przegl. lek., Krakow, 25: 1; 17; 47; 63; 78; 127, 1886.
54. Zur operativen Behandlung des Empyems der Highmorschöhle. (Operative treatment of empyema of the antrum of Highmore.) Chirurgenkongress, 1886. Also: Centralbl. f. Chir., 13, 1886. Also: Pamietnika towarz lek., Warszawa, 82: 261-262, 1886. Also: 8°, Leipzig, 1886, in A. Also: Arch. f. klin. Chir., 34: 626-634, 1887. Also: Zeitschr. f. Heilk., Prag., 7: 257-265, 1887. Also: 10 pp., 1 pl., 8°, Berlin, Hirschwald, 1887, in A.
55. O fizyologicznem zachowaniu sie przełyku i mechanizmie połknięcia u człowieka. (Physiological behavior of the pharynx and the mechanism of swallowing in man.) With N. Czubulski. Krakow, Ak. (Mat.-Przyrod.) Rozpr., 15: 203-210, 1887.
56. Opatrunek trwały i leczenie ran pod wilgotnym strupam krwi. (Permanent dressings and treatment of wounds by scabbing.) Przegl. lek., Krakow, 26: 21; 29, 1887.
57. Zur operativen Behandlung der Pylorusstenose. (Operative treatment of pyloric stenosis.) Zur operativen Behandlung des stenosierenden Magengeschwürs. (Operative treatment of stenosing ulcers of the stomach.) Chirurgenkongress, 1887. Also: Centralbl. f. Chir., 14, 1887. Also: 8°, Leipzig, 1887, in A. Also: Arch. f. klin. Chir., 37: 79-90, 1888. Also: 12 pp., 8°, Berlin, Hirschwald, 1888, in A.
58. Über extrabukkale temporäre Resektionen des Unterkieferastes als Vorakt der seitlichen Pharyngotomie und der Resektion des 3. Trigeminusastes. (Extrabuccal temporary resection of the ramus of the lower jaw previous to lateral pharyngotomy and resection of 3rd branch of fifth cranial nerve.) Abstract of Society report in Berl. klin. Wochensch., 39: 736, 1887.
59. Erfahrungen über den Dauerverband und die Wundheilung ohne Drainage. (Experiences in permanent dressing

and wound treatment without drainage.) *Klin. Jahrb.*, 1, 1888.

60. Zur operativen Behandlung des Prolapsus recti et coli invaginati. (Operative treatment of prolapse of rectum and intussusception of colon.) *Chirurgenkongress*, 1888. Also: *Verhandl. d. deutsch. Gesellsch. f. Chir.*, Berl., 17: pt. 2, 294-317, 1888. Also: *Centralbl. f. Chir.*, 15, 1888. Also: 8°, Leipzig, 1888, in A. Also: *Arch. f. klin. Chir.*, 38: 74-97, 1889.
61. Weitere Erfahrungen über die operative Behandlung der Perforationsperitonitis. (Further experiences in the operative treatment of perforative peritonitis.) *Chirurgenkongress*, 1889. Also: *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 18: pt. 2, 303-331, 1889. Also: *Centralbl. f. Chir.*, 1889. Also: *Arch. f. klin. Chir.*, 39: 756-784, 1889. Also: *Wien. med. Bl.*, 39: 889, 1889.
62. Zur Behandlung der Pseudarthrose. (Treatment of pseudoarthrosis.) *Chirurgenkongress*, 1889. Also: *Centralbl. f. Chir.*, 1889.
63. Laparotomie wegen Wanderniere, Bestreichen des Peritonealüberzuges derselben mit Jodoformkollodium, Reposition der Niere, Heilung in 2 Fällen durch Verwachsung mit dem benachbarten Peritoneum. (Laparotomy for floating kidney, coating its peritoneal covering with iodoform-collodium, replacing the kidney. Cure in 2 cases by adhesions with neighboring peritoneum.) *Zeitschrift f. Geb.*, 19, 1890.
64. Infusion of salt solution and transfusion of blood in acute anemia; their relative value. Translated by O. K. Newell. 16 pp., 8°, Boston, Parkhill, 1890, in A & C.
65. Über den Hämoglobingehalt des Blutes bei chirurgischen Erkrankungen, mit besonderer Rücksicht auf den Wiedersatz bei Blutverlusten. (Hemoglobin content of the blood in surgical diseases, with special regard to replacement of blood loss.) *Chirurgenkongress*, 1890. Also: *Wien. med. Wochensch.*, 40: 803-804, 1890. Also: *Centralbl. f. Chir.*, 1890.

66. Die bisherigen Erfolge des Kochschen Heilverfahrens gegen Tuberkulose. (Results, up to the present time, of Koch's method of treatment of tuberculosis.) Deutsch. med. Wochensch., 17, 1891. Also: 25 pp., 8°, Leipzig, Thieme, 1891, in A.
67. Über die in der Kgl. chirurgischen Klinik mit dem Kochschen Heilmittel gewonnenen Erfahrungen. (Experiences in the Kgl. surgical clinic with Koch's treatment.) Jahresb. d. Schles. Gesellsch. f. Vater. Kult., 1891, Bresl., 69: med. abth., 18-22, 1892.
68. Über die Behandlung brandiger Brüche. (Treatment of gangrenous herniae.) Naturf.-Vers. Halle, 1891. Also: Berl. klin. Wochensch., 29: 209; 249; 277; 305, 1892.
69. Zur Feier der 25 jährigen Lehrthätigkeit Theodore Billroth's in Wien. (Commemoration of Theodore Billroth's 25 years as a teacher in Vienna.) Deutsche med. Wochensch., 18: 913-915, 1892.
70. Die heutige Chirurgie und der chirurgische Unterricht. (Present day surgery and surgical instruction.) Klin. Jahrb., Berl., 4: 24-44, 1892.
71. Über eine eigenartige symmetrische Erkrankung der Thränen-und Mundspeicheldrüsen. (A peculiar symmetrical disease of the lacrymal and salivary glands.) Beitr. z. Chir. Festschr. f. Theodor Billroth, Stuttg., pp. 610-630, 1892. Also: 22 pp., 8°, Stuttgart, Enke, 1892, in A.
72. Paul Michelson. Biography. Deutsch. med. Wochensch., 18, 1892. Also: 2 pp., 8°, Leipzig, 1892, in A.
73. Demonstration eines Falles von Thoraxresektion wegen Chondrosarkoms. (Demonstration of a case of resection of the thorax for chondrosarcoma.) Naturf. Vers. Halle, 1892.
74. Atlas der Krankheiten der Mund- und Rachenhöhle. (Atlas of diseases of mouth and pharyngeal cavity.) With P. Michelson. 89 l., 44 pl., roy. 8°, Berlin, Hirschwald, 1892, in A, B, C and E.
75. Bibliotheca medica. Hrsg. Kocher, König & Mikulicz, 1893.

76. Nachträgliche Bemerkungen zur Witzelschen Methode der Gastrostomie. (Additional observations on Witzel's method of gastrostomy.) Berl. klin. Wochensch., 30: 1, 1893.
77. Die Entwicklung der Chirurgie an den deutschen Universitäten. Werk zur Chicagoer Weltausstellung: "Die deutschen Universitäten." (The development of surgery in German universities. A work for the Chicago Exposition: "The German Universities.") Berlin, Asher, 1893.
78. Article on operation for bleeding gastric ulcer (gastric hemorrhage). Congress of French Surgeons, 1893.
79. Stereoskopischer medizinischer Atlas. (Stereoscopic medical atlas.) With A. Neisser & Partsch. Leipzig, Barth, 1894.
80. Der heutige Stand der Magen Chirurgie. (Present state of stomach surgery.) Allgem. med. Centralzeit., 1894.
81. Theodor Billroth. Berl. klin. Wochensch., 1894.
82. Über den Ersatz von grösseren Hautdefekten durch Transplantation ungestielter Hautlappen nach der Methode von Krause. (Substitution of large skin defects by transplantation of a sessile skin flap by the method of Krause.) Dermatologenkongress, 1894.
83. Zur chirurgischen Behandlung der Hautmäler. (Surgical treatment of moles.) Ibid. Also: 3 pp., 8°, Wien, 1894, in C.
84. Zur Behandlung der Tuberkulose mit Stauungshyperämie nach Bier. (Treatment of tuberculosis with passive hyperemia according to Bier.) Centralbl. f. Chir., 21: 265-273, 1894.
85. Chloroform oder Aether? (Chloroform or ether?) Berl. klin. Wochensch., 31: 1035-1039, 1894. Also: 13 pp., 8°, Berlin, 1894, in C.
86. Die unblutige Reduktion der angeborenen Hüftverrenkung. (Bloodless reduction of congenital dislocation of the hip.) Arch. f. klin. Chir., 49: 368-386, 1894. Die blutige und unblutige Reduktion der congenitalen Hüftluxation. (Open and closed reduction of congenital dislocation of

the hip.) Attid. XI Cong. med. internaz. 1894, Roma, 4: chirurg., 411, 1895.

87. Über die Exstirpation des Kopfnickers beim muskulären Schiefhals, nebst Bemerkungen zur Pathologie dieses Leidens. (Extirpation of sterno-mastoid for muscular torticollis, with remarks on the pathology of this affection.) Centralbl. f. Chir., 22: 1-9, 1895.
88. Über Thymusfütterung bei Kropf und Basedow'scher Krankheit. (Feeding of thymus in goiter and Basedow's disease.) Berl. klin. Wochensch., 32: 342-346, 1895. Also: 12 pp., 8°, Berlin, 1895, in A.
89. Die chirurgische Behandlung der Basedow'schen Krankheit. (Surgical treatment of Basedow's disease.) Chirurgenkongress, 1895. Also: Verhandl. d. deutsch. Gesellsch. f. Chir., 24: 21-29, 1895. Also: Ber. u. d. Verhandl. d. Gesellsch. f. Chir., 24: 67-72, 1895.
90. Surgery of the stomach. Med. Week, Par., 3: 195, 1895.
91. Über ausgedehnte Resektionen der langen Röhrenknochen wegen maligner Geschwülste. (Extensive resection of the long bones for malignant tumors.) Verhandl. d. deutsch. Gesellsch. f. Chir., 24: pt. 2, 350-365, 1895; discussion, pt. 1, 104. Also: Arch. f. klin. Chir., 50: 660-675, 1895. Also: Ber. u. d. Verhandl. d. deutsch. Gesellsch. f. Chir., 24: 130, 1895. Also: Chirurgenkongress, 1895. Also: 17 pp., 1 pl., 8°, Berlin, 1895, in A.
92. Bericht über 103 Operationen am Magen. (Report on 103 Operations on the stomach.) Chirurgenkongress, 1895. Also: Verhandl. d. deutsch. Gesellsch. f. Chir., 24: pt. 2, 737-767, 1895. Also: Arch. f. klin. Chir., 51: 9-39, 1895. Also, abstr.: Ber. u. d. Verhandl. d. deutsch. Gesellsch. f. Chir., 24: 72-76, 1895. Also: Toledo Med. & Surg. Reporter, 9: 527, 1896. Also: 31 pp., 8°, Berlin, 1896, in A.
93. Weitere Erfahrungen über die unblutige Reduktion der angeborenen Hüftverrenkung. (Further experiences with bloodless reduction of congenital dislocation of the hip.) Chirurgenkongress, 1896. Also: Centralbl. f. Chir., 1896.

94. Ein neues chirurgisches Taschenbesteck, insbesondere für den Feldgebrauch bestimmt. (A new surgical pocket dressing-case, especially designed for military use.) Deutsch. militärärztl. Zeitschr., 25: 156-161, 1896.
95. Local diseases of the mouth. With W. Kümmel. In Twentieth Century Practice of Medicine. N. Y., Wood, 9: 1-94, 1897.
 (Same) Die Krankheiten des Mundes. With contributions by Czerny and Schaeffer. With W. Kümmel. ix, 253 pp., 2 pl., 8°, Jena, Fischer, 1898, in A, B, C and D.
 (Same) 2. ed., vii, 295 pp., 8°, Jena, Fischer, 1909, in A & C.
 (Same) 3. ed., vii, 320 pp., 8°, Jena, Fischer, 1912, in A & C.
 (Same) 4. ed., vii, 338 pp., 8°, Jena, Fischer, 1922, in C & D.
96. Das Operieren in sterilisierten Zwirnhandschuhen und mit Mundbinde; ein Beitrag zur Sicherung des aseptischen Verlaufs von Operationswunden. (Operating in sterilized linen gloves and with a mouth covering; a contribution to securing an aseptic course in operative incisions.) Centralbl. f. Chir., 24: 713-717, 1897. Also: 4 pp., 8°, Leipzig, 1897, in A.
97. Über Versuche, die aseptische Wundbehandlung zu einer wirklich keimfreien Methode zu vervollkommenen. (Research on improving aseptic treatment of wounds by a practical germ-free method.) Deutsch. med. Wochenschr., 23: 409-413, 1897. Also: 13 pp., 8°, Leipzig, Thieme, 1897, in A.
98. Neubildungen des Rachens und des Nasenrachenraumes. (New growths of the pharynx and naso-pharynx.) In P. Heymann's Handbuch der Laryngologie und Rhinologie, Wien, 2: 385-445, 1897.
99. Die chirurgische Behandlung des chronischen Magengeschwürs. (Surgical treatment of chronic gastric ulcers.) Chirurgenkongress, 1897. Also: Centralbl. f. Chir., 24: 69-98, 1897. Also: Mitteil. a. d. Grenzgeb. d. Med. u.

- Chir., 2: 184-272, 1897. Also: Arch. f. klin. Chir., 55, 1897. Also: Berl. klin. Wochensch., 34: 488; 522; 561; 640, 1897. Also, abstr.: Deutsch. med. Wochensch., 22: Ver.-Beil., 83, 1897. Also, abstr.: Jahresb. d. schles. Gesellsch. f. vaterl. Cult., 1896, Bresl., 74; 1. Abt., Med. Sect., 115-122, 1897. Also: 37 pp., 8°, Berlin, 1897, in A.
100. Über die neuesten Bestrebungen, die aseptische Wundbehandlung zu vervollkommen. (The latest attempts to improve aseptic wound treatment.) Chirurgenkongress, 1898. Also: Centralbl. f. Chir., 1898. Also: Arch. f. klin. Chir., 57: 243-279, 1898. Also: Verhandl. d. deutsch. Gesellsch. f. Chir., 27: pt. 2, 1-37, 1898. Also: 37 pp., 8°, Berlin, 1898, in A.
101. Beiträge zur Technik der Operation des Magenkarzinoms. (Contributions to the technique of operation for carcinoma of the stomach.) Chirurgenkongress, 1898. Also: Arch. f. klin. Chir., 57: 524-532, 1898. Also: Verhandl. d. deutsch. Gesellsch. f. Chir., 27: pt. 2, 252-260, 1898. Also, abstr.: Centralbl. f. Chir., 25: 118-121, 1898. Also: 10 pp., 8°, Berlin, 1898, in A.
102. Die heutige Chirurgie und der chirurgische Unterricht. (Modern surgery and surgical instruction.) Klin. Jahrbuch, 4: 24, 1898.
103. Discussionsbemerkungen zu dem Vortrage des Herren Dr. Tietze (über) die chirurgische Behandlung der acuten Peritonitis. (Discussion of report of Dr. Tietze on surgical treatment of acute peritonitis.) Allg. med. Centr.-Zeitg., Berl., 67, 1898. Also: 1 l., 8°, Berlin, 1898, in A.
104. Discussionsbemerkungen zu dem Vortrage des Herren Prof. Kolaczek zur Frage der totalen Magenresection. (Discussion of report of Prof. Kolaczek on question of total resection of stomach.) Allg. med. Centr.-Zeitg., Berl., 67, 1898. Also: 1 l., 8°, Berlin, 1898, in A.
105. Über den heutige Stand der Chirurgie der Gallenwege. (Modern attitude toward surgery of the bile-ducts.) Allg. med. Centr.-Zeitg., 68, 1899. Also: 3 pp., 8°, Berlin, 1899, in A.

106. Zur Operation der angeborenen Blasenspalte. (Operation for congenital ectopia of the bladder.) *Centralbl. f. Chir.*, 26, 1899. Also: 1 l., 8°, Leipzig, 1899, in A.
107. Die Desinfektion der Haut und Hände mittels Seifenspiritus. (Disinfection of skin and hands by means of solution of soap in spirits.) *Deutsch. med. Wochensch.*, 25, 1899. Also: 9 pp., 8°, Leipzig, Thieme, 1899, in A.
108. Handbuch der praktischen Chirurgie. By Bergman, Bruns & Mikulicz. (Handbook of practical surgery.) 4 vols., 8°, Stuttgart, 1899-1900.
 (Same) *Trattato di chirurgia pratica*. Milano. Soc. edit. libr., 1901.
 (Same) 2. ed., in German, 1903.
 (Same) In English, trans. by Bull et al., 5 vols., N. Y. Lea, 1904.
 (Same) 4. ed., in German, Stuttgart, 1913-14.
 (Same) 5. ed., in German, Stuttgart, 1921-24.
 (Same) 6. ed., in German, 6 vols. in 7, Stuttgart, F. Enke, 1926-1931.
109. Discussionsbemerkungen des Herren Dr. Gottstein über seltene Erkrankungen der Speiseröhre und deren diagnostische Feststellung durch das Oesophagoskop. (Discussion of Dr. Gottstein on rare diseases of the esophagus and their diagnostic determination by the esophagoscope.) *Allg. med. Centr.-Zeitg.*, Berl., 69, 1900. Also: 1 l., 8°, Berlin, 1900, in A.
110. Die Verletzungen und Erkrankungen des Magens. (Injuries and diseases of the stomach.) With W. Kausch. *Handb. d. prakt. Chir.*, Stuttg., 3: 234-316; 392-475, 1900.
111. Technik der Operationen am Magen-Darm-Kanal. (Technique of operations on the stomach and intestines.) With W. Kausch. *Ibid.*, 168-234.
112. Über Ileus. (Ileus.) *Therapie d. Gegenwart*, n. s., 2: 438-450, 1900. Also: *Allg. med. Centr.-Zeitg.*, 69, 1900. Also: 6 pp., 8°, Berlin, 1900. Also: 13 pp., roy. 8°, Berl. & Wien, 1900, in A.

113. Über die Narkose. Die deutsche Klinik am Eingange des 20. Jahrhunderts von v. Leyden und F. Klemperer. (Narcosis. The German Clinic at the beginning of the 20th century—.) 8, 1901. Also: 36 pp., roy. 8°, Berlin & Wien, 1901, in A.
114. Die Methoden der Schmerzbetäubung und ihre gegenseitige Abgrenzung. (Methods of pain control and their respective limitations.) Chirurgenkongress, 1901. Also: Arch. f. klin. Chir., 64, 1901. Also: 34 pp., 8°, Berlin, 1901, in A.
115. Discussionsbemerkungen zu dem Vortrage des Herren Poufick über die Beziehungen der Scrophulose zur Tuberculose. (Remarks in discussion of the report of Herr Poufick on relation of scrofula to tuberculosis.) Allg. med. Centr.-Zeitg., Berl., 69, 1901. Also: 1 l., 8°, Berlin, 1901, in A.
116. Zur operativen Behandlungen der Basedow'schen Krankheit. (Operative treatment of Basedow's disease.) Allg. med. Centr.-Zeitg., 69, 1901. Also: 3 pp., 8°, Berlin, 1901, in A.
117. Über Thyreoidismus bei einfachem Kropf. (Thyreoidismus in simple goitre.) With G. Reinbach. Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 8: 247-265, 1901. Also, abstr.: Centralbl. f. Chir., 1: 52-54, 1902. Also: pp. 247-265, 8°, Jena, Fischer, 1901, in A.
118. Chirurgische Erfahrungen über Magencarcinom. (Surgical experiences with carcinoma of stomach.) Centralbl. f. Chir., 28: 1197-1200, 1901. Also, abstr.: Versam. Deut. Naturf. u. Ärzte, sek. f. Chir.
119. Orthopädische Gymnastik gegen Rückgratsverkrümmungen und schlechte Körperhaltung. (Orthopedic gymnastics for curvature of spine and bad posture.) With Tomaszewski. xlii, 103 pp., 8°, Jena, Fischer, 1902, in A and D.
(Same) 2. ed., 1904, in A. (Same) 3. ed., 1908, in A.
(Same) 4. ed., 1917.
120. Ein Fall von Ureterstein. (A case of ureteral stone.) Schles. Gesellsch. f. vaterländ. Kultur in Breslau, Nov. 28, 1902.

121. Contribution to the treatment of fractured patella. Brit. Med. Jour., 2: 1828-1831, 1902.
122. Ausgedehnte Darmresektion bei Ileocoloninvagination. (Extensive resection of intestine for ileo-colic intussusception.) Allg. med. Centr.-Zeitg., 1902.
123. Demonstration eines mit Erfolg operierten Falles von Oesophagusdivertikel. (Demonstration of a case of diverticulum of the esophagus with operative result.) Ibid.
124. Chirurgische Erfahrungen über das Darmcarcinom. (Surgical experiences with intestinal carcinoma.) Chirurgenkongress, 1902. Also: Arch. f. klin. Chir., 69: 28-47, 1903. Also: La clinica moderna, Zaragoza, 1903. Also, abstr.: Centralbl. f. Chir., 1: 104-107, 1902.
125. Ein operativ geheilter Fall von Kardiospasmus. (A case of cardiospasm cured by operation.) Allg. med. Centr.-Zeitg., 1903.
126. Allgemeines über Laparotomie. (Generalities on laparotomy.) With W. Kausch. Handb. d. prakt. Chir., (Bergmann), 2 Auf., Stuttg, 1903, in C.
127. Verletzungen und Erkrankungen des Magens und Darms. (Injuries and diseases of the stomach and intestines.) With W. Kausch. Handb. d. prakt. Chir., (Bergmann), 2 Auf., Stuttg., 3: 143-389, 1903. Also: 247 pp., 8°, Stuttgart, 1903, in C.
128. Über einen mit Röntgenstrahlen erfolgreich behandelten Fall von Brustdrüsenkrebs. (A case of cancer of the mammary gland with results of treatment with x-ray radiation.) Beitr. z. klin. Chir., 37: 676-697, 1903.
129. Small contributions to the surgery of the intestinal tract. Trans. Amer. Surg. Assn., Phila., 21: 124-134, 1903. Also: Bost. Med. & Surg. Jour., 148: 608-611, 1903.
130. Über die Skoliose. (Scoliosis.) Kinder-Arzt., Leipzig, 14: 121-129, 1903. Also: Aertzl. Rundschau., München, 13: 340-343, 1903.
131. Max Schade; Alfred Kast. Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 11, 1903.

132. Über den heutigen Stand der Chirurgie des Pankreas, mit besonderer Rücksicht auf die Verletzungen und Entzündungen des Organes. (The modern attitude toward surgery of the pancreas, with special regard to injuries and inflammations of the organ.) Ibid., 12: 1-24. Also: Trans. Congr. Amer. Phys. & Surg., 6: 55-79; 98-104, 1903.
133. Surgery of the pancreas. Ann. Surg., 38: 1-29, 1903.
134. Beiträge zur Physiologie der Speiseröhre und der Kardial. (Contributions to the physiology of esophagus and cardia.) Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 12: 569-601, 1903.
135. Cystische Degeneration der langen Röhrenknochen. (Cystic degeneration of long bones.) N. Y. Med. W., 16: 83-90, 1904.
136. Zur Pathologie und Therapie des Kardiospasmus. (Pathology and therapy of cardiospasm.) Deutsch. med. Wochenschr. 30: 17-19; 50-54, 1904.
137. Einiges über Naht und Nahtmaterial. (Briefly on suturing and suture material.) Ibid., 415; 1463.
138. Über Operationen in der Brusthöhle mit Hilfe der Sauerbruchschen Kammer. (Operations in thoracic cavity with aid of Sauerbruch's air-chamber.) Ibid., 530; 577. Also: Chirurgenkongress, 1904.
139. Die heutige Magen- und Darmchirurgie und ihre Bedeutung für den inneren Arzt. (Modern surgery on stomach and intestines and its significance for the internist.) Deutsch. Klinik am Eingange des 20. Jahrhunderts, 8: 929-952, 1904.
140. Zur Pathologie der Gelenkkontrakturen. (Pathology of joint contractures.) Zeitsch. f. orthopäd. Chir., 13: 233-241, 1904.
141. Multiple Knochentumoren. (Multiple bone tumors.) Naturf.-Vers. Breslau, 1904.
142. Versuche über Resistenzvermehrung des Peritoneums gegen Infektion bei Magen- und Darmoperationen. (Experiments on increasing the resistance of the peritoneum to

- infection in stomach and intestinal operations.) Chirurgenkongress, 1904. Also: Arch. f. klin. Chir., 73: 347-368, 1904.
143. The Cavendish Lecture on experiments on the immunization against infection of operation wounds, especially of the peritoneum. Lancet, 1904. Also: West London Med. Jour., 9: 157-180, 1904.
144. Über perineale Prostatektomie. (Perineal prostatectomy.) Naturf.-Vers. Breslau, 1904. Also: München. med. Wochensch., 51: 1765, 1904.
145. Sackartige Dilatation des Oesophagus. (Cystic dilatation of esophagus.) Allg. med. Centr.-Zeitg., 1904.
146. Chirurgische Universitätsklinik Breslau. Deutsche Unterrichtsausstellung, Medizin. Weltausstellung, St. Louis, 1904. (University Surgical Clinic at Breslau. Demonstration of German Teaching in Medicine. World's Fair, St. Louis, 1904.
147. Die Bedeutung der Röntgenstrahlen für die Chirurgie. (The importance of x-ray radiation to surgery.) Deutsch. med. Wochensch., 31: 657-663, 1905.

BIOGRAPHIES

- Biography by Sauerbruch. München. med. Wochensch., 52: 1297-1300, 1905.
- Biography by Eiselsberg. Wien. klin. Wochensch., 18: 671-674, 1905. Also: Centralbl. f. Chir., 32: No. 26, 1905.
- Obituary by A. Wolfer. Prag. med. Wochensch., 30: 366-368, 1905.
- Obituary by M. Blumberg. Deutsch. med. Presse, 9: 90, 1905.
- Obituary. Boston Med. & Surg. Jour., 153: 64, 1905.
- Obituary by J. F. Lehman. München. med. Wochensch., No. 27, 1905.
- Biography by W. Ausschütz. Berl. klin. Wochensch., 42: 1163-1165, 1905.
- Biography. Brit. Med. Jour., 2: 49, 1905.
- Biography by D. G. Zesas. Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Jena, 8: 449-453, 1905.

- Biography by Czerny. Deutsch. med. Wochensch., 31: 1039, 1905.
- Biography by J. S. Ibid., 999.
- Biography. Jour. Amer. Med. Assn., 45: 58, 1905.
- Biography. Lancet, 2: 122, 1905.
- Biography by Pels-Leusden. Med. Klin., Berl., 1: 734, 1905.
- Biography by Naunyn. Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 14: i-vi, 1905.
- Biography by Poufick. Jahresb. d. Schles. Gesellsch. f. vaterl. Cult., 1905, Breslau, pp. 115-118, 1906.
- Biography by W. Krausch. Johann von Mikulicz-Radecki. Sein Leben und seine Bedeutung. Gedenkband für J. von Mikulicz—Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 3 suppl., Jena, Fischer, pp. 1-58, 1907. Bibliography, pp. 58-64.
- Festrede bei der Enthüllung des Mikulicz-Denkmales in Breslau am 27 Mai 1909. Berl. klin. Wochensch., 46: 1495, 1909.
- Mikulicz's drain. Amer. Jour. Surg., 8: 1103, 1930.
- Twenty-fifth anniversary of death of Mikulicz. By H. Küttner. Beitr. z. klin. Chir., 150: 1-6, 1930.

INDEX TO BIBLIOGRAPHY

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MIKULICZ'S DISEASE

Mikulicz reported a single case of chronic hypertrophy of the lacrymal and salivary glands at a meeting of the Society for Scientific Medicine at Königsberg in 1888. He carefully perused the literature for corresponding cases and four years later, at the dedication of a volume of medical articles to his former chief, Theodor Billroth, published a detailed description of the patient with illustrations and reviewed a few other cases having some similar characteristics reported by other observers.

In the original case swelling of the lacrymal glands appeared first, followed by swelling in the submaxillary and parotid regions; only the swelling near the eyes gave any disturbance, and then interfered with vision only because of size. After removal of about two-thirds of the lacrymal tumors, the swelling reappeared in about two (?) months. Again surgical removal was instituted, this time including the submaxillary glands also. Two months later the patient reported himself in good health but a few days later was stricken with what was probably appendicitis and died in nine days. During this last illness all the swellings practically disappeared.

Microscopically the portion of gland removed revealed "a massive, small-cell infiltration of the interstitial connective tissue," "the true parenchyma of the glands playing an entirely passive rôle."

In his review of several cases from the literature, Mikulicz shows that most of them do not correspond to his case; some are of acute swellings or inflammations of the lacrymal gland alone, others concern leukemic or tuberculous involvement of salivary and lacrymal glands or of lymph nodes of the face or neck. Finally, in summing up his knowledge, Mikulicz theorizes as to the interrelation between lacrymal and salivary gland disease extending by way of buccal and nasal mucosa. He believed the causative factor to be "an infectious or parasitic process in the broadest sense of the word."

Following the recognition of this disease, many case reports appeared. Then in 1907, Napp, O. (*Ztschr. f. Augenh.*, 17: 513) declared the condition to be simply a symptom complex that might be produced by any one of several causes, such as leukemia, pseudoleukemia, atypical lymphomatosis and tuber-

culosis. An important milestone in the study of the condition was an article by Howard, C. P. (*Internat. Clin.*, 1: 30, 1900) who classified all the cases he could find in the literature into three groups, (1) Mikulicz's disease proper, (2) pseudoleukemia and (3) leukemia.

In 1927 Schaffer and Jacobsen (*Am. J. Dis. Child.*, 34: 327) reviewed all cases of this syndrome seen at the Johns Hopkins Hospital and divided them into two groups: (1) symptomatic and (2) Mikulicz's disease proper. They maintain that the syndrome can occur in leukemia, lymphosarcoma and tuberculosis, possibly in syphilis, but that Mikulicz's disease proper should be reserved for those cases where a thorough search fails to reveal any underlying or associated disease factors. (Editorial, *Jour. Amer. Med. Assn.*, 89, 1429, 1927.)

Thus we stand today exactly where Mikulicz did in 1892 when he called for help in solving the riddle of this condition. We know only that the disease seems to be a low-grade infection of the lacrymal and salivary glands, extending over a long period with possible spontaneous termination and never causing death.

The translation here given was made by Dr. W. de Rouville.



Ueber eine eigenartige symmetrische Erkrankung der Thränen- und Mundspeicheldrüsen

VON

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Mit Tafel IX und 5 Holzschnitten

From Beiträge zur Chirurgie. Festschrift gewidmet Theodor Billroth von seinen dankbaren Schülern zu feier des vollendeten fünfzigsten Semesters seines akademischen Wirkens in Wien. Stuttgart, Enke, 1892

IN DER Sitzung vom 23. Januar 1888 stellte ich im Verein für wissenschaftliche Heilkunde zu Königsberg¹ einen Fall vor der ein eigentümliches, mir bis dahin unbekanntes Krankheitsbild darbot. Beide Thränendrüsen und sämtliche Mundspeicheldrüsen waren in symmetrischer Weise zu Geschwülsten umgewandelt, die sich aus dem normalen Lager dieser Organe stark hervordrängten und dadurch das Gesicht des Kranken in auffallender Weise entstellten. Die Geschwülste waren allmählich entstanden; sie waren zur Zeit der Untersuchung von derber Konsistenz, schmerzlos, ohne Spur von entzündlichen Erscheinungen. Im übrigen waren an dem Träger dieser Tumoren keine krankhaften Veränderungen nachzuweisen.

Die Deutung dieses Krankheitsfalles setzte mich in die grösste Verlegenheit, denn er passte nirgends in den Rahmen der bisher bekannten und benannten Krankheiten. Auch fand ich in der

¹ Berliner klin. Wochenschrift 1888, 759.

Litteratur nicht eine einzige der meinigen analoge Beobachtung verzeichnet. Ich hatte die Hoffnung, dass mir der Zufall einen zweiten, ähnlichen Fall in die Hände spielen und dadurch die Auffassung des Krankheitsbildes erleichtern werde. Indessen scheint die betreffende Affektion sehr selten zu sein, so dass ich diese Hoffnung wohl aufgeben muss. Ueberdies sind in der Zwischenzeit von anderen (p. 611) Beobachtern mehrere Fälle mitgeteilt worden, die dem meinigen entweder völlig gleichen oder doch so ähnlich sind, dass sie zur Beurteilung des vorliegenden Krankheitsprozesses herangezogen werden dürfen.

Aus diesem Grunde habe ich mich entschlossen, meinen Fall schon heute ausführlich mitzuteilen.

KRANKENGESCHICHTE

Der 42 jährige, verheiratete Eigenkätchner (kleiner Bauer) Christof Kalweit aus Marienwalde in Ostpreussen hat vor 20 Jahren eine Lungenentzündung durchgemacht; sonst will er stets gesund gewesen sein. Vor 7 Monaten, im Juni 1887, bemerkte er, dass beide obere Augenlider zu schwellen begannen; er hatte dabei weder Schmerzen noch sonstige Beschwerden, nur wurde mit zunehmender Schwellung das Oeffnen der Lider erschwert. Später verengte sich die Lidspalte derart, dass er im Sehen behindert wurde. Bald darauf entwickelte sich unter beiden Kieferwinkeln eine ebenfalls schmerzlose Geschwulst, die im weiteren Verlaufe beim Essen und Sprechen hinderlich wurde. Ueber die Zeit der Entwicklung der anderen Anschwellungen vermag Patient nichts anzugeben, jedenfalls zeigten sie sich erst später. Nur die Beeinträchtigung im Gebrauch der Augen beunruhigte den Kranken und führte ihn zu einem Arzte, der ihm eine innere Medizin verschrieb. Als dies erfolglos blieb, suchte er in der chirurgischen Klinik in Königsberg Hilfe.

Befund am 13. Januar 1888. Kräftig gebauter, gut genährter Mann von sonst gesundem Aussehen. In den inneren Organen keine Abweichungen nachweisbar. Insbesondere zeigen Leber, Milz und Nieren keine Veränderungen; Urin eiweissfrei. Pankreas nicht zu palpieren. Prostata nicht vergrössert. Nirgends nachweisbare Lymphdrüsenanschwellungen. Im Blut keine auffal-

lenden Veränderungen, insbesondere keine Leukocythose. Sehnen- und Hautreflexe normal. Temperatur und Puls normal.

In auffallender Weise erscheint das Gesicht durch symmetrische Anschwellungen im Bereich der oberen Augenlider, der Parotis

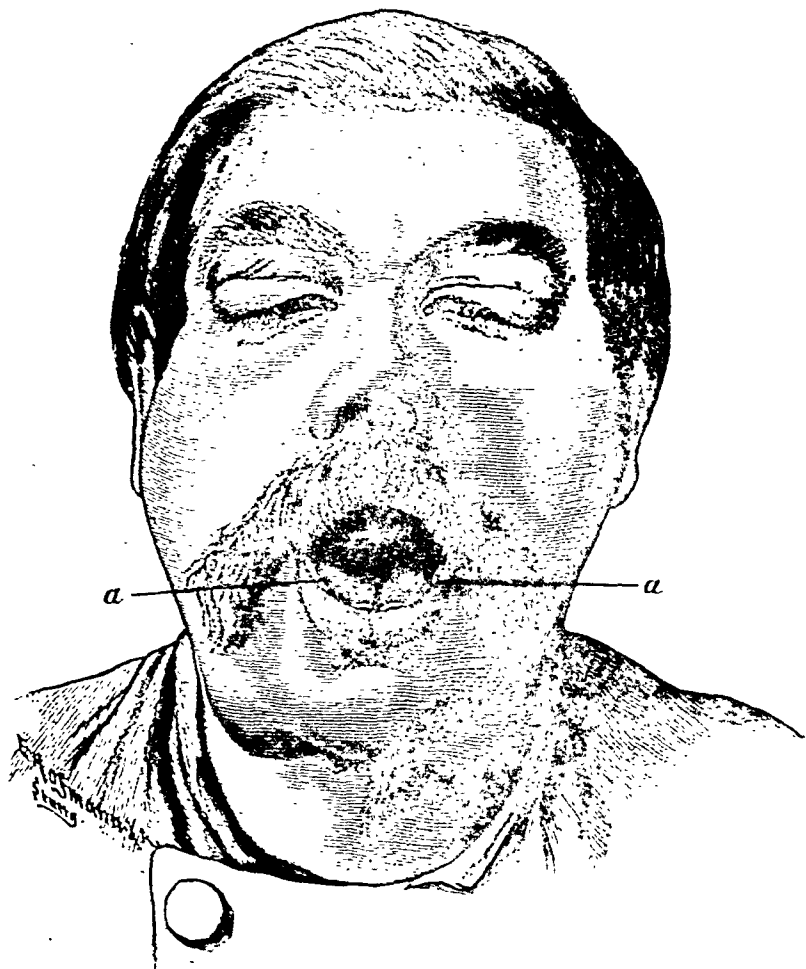


Fig. A

und der Submaxillargegend verändert. (Siehe beistehende Abbildung Fig. A.)

Die oberen Augenlider hängen, besonders in ihrer lateralen Hälfte, so weit herunter, dass die Lidspalte auf einen schmalen,

dreieckigen Raum reduziert erscheint, dessen Basis die zwei inneren Drittel des unteren Lidrandes bilden. Im äusseren Drittel berühren sich die beiden Lidränder vollständig. Pat. vermag selbst unter (p. 612) starker Anstrengung das obere Lid nicht merklich höher zu heben. Infolgedessen bleibt dauernd das grössere, obere äussere Segment der Iris und Pupille vom oberen Lid verdeckt. Wohl infolgedessen hat sich ein Strabismus convergens entwickelt, durch welchen die Pupillen in den relativ weiteren medialen Teil der Lidspalte eingestellt werden.

Die äusseren zwei Drittel der oberen Augenlider sind ausserdem halbkugelig nach vorn und aussen gewölbt, so dass hier die mitt-



Fig. B

lere Lidfalte fast verstrichen erscheint. Bei der Palpation findet man hier unter der Lidhaut einen kleinhöckerigen, derben Tumor von quer ovaler Gestalt, der sich bis an den Orbitalrand verfolgen lässt. Der Tumor selbst ist wenig beweglich, die leicht ödermatöse Lidhaut über demselben dagegen leicht verschiebbar (p. 613). Wird das obere Augenlid mit dem Finger stark in die Höhe gezogen, so erscheint die äussere Hälfte der Uebergangsfalte durch den beschriebenen Tumor so weit hervorge drängt, dass sie bis nahe an den Cornealrand reicht. (Vergl. nebenstehende Abbildung Fig. B.) Conjunctiva selbst leicht gerötet und etwas verdickt. Die Bulbi etwas nach innen und vorn dislociert, im

übrigen keine krankhaften Veränderungen an ihnen nachweisbar. Sehvermögen ungestört.

Die Parotisgegend beiderseits von einer flach gewölbten, einheitlichen Geschwulst eingenommen, welche ihrem Sitze nach genau der Lage der Ohrspeicheldrüse entspricht; sie dehnt sich nach vorn bis in die Mitte der Wange aus, lässt sich in die Nische zwischen Kieferast und Warzenfortsatz verfolgen und hebt das Ohrläppchen deutlich ab. Konsistenz derb elastisch. Ihre Oberfläche ist scheinbar glatt, die Haut darüber wenig verschiebbar.

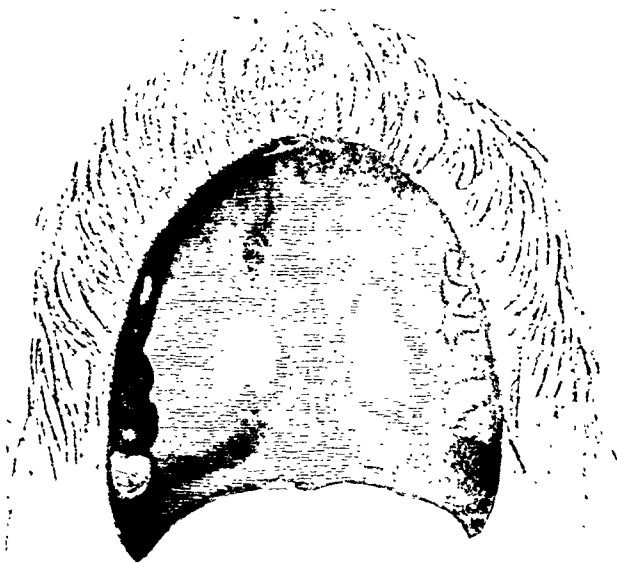


Fig. C

Unter jedem Kieferwinkel ragt eine circa hühnereigrosse, von normaler, verschiebbarer Haut bedeckte Geschwulst hervor. Sie ist etwas verschiebbar, von derber Konsistenz; ihre Oberfläche lässt stellenweise flache Höcker erkennen. Die beiden Tumoren stossen in der Mittellinie fast zusammen.

Oeffnet Pat. den Mund, so fallen zunächst zwei den Sublingualdrüsen entsprechende Tumoren auf. Sie präsentieren sich als zwei längliche Geschwülste, welche, in Form und Grösse einer auf die Kante gestellten Mandel, den Boden der Mundhöhle zu

beiden Seiten des Frenulum linguae einnehmen. (Siehe Fig. A a-a.) Sie reichen bis in die Höhe der Zahnkronen und lagern sich so zwischen die Spitze der ruhenden Zunge und die Zahnreihe. Die Schleimhaut über den Tumoren leicht geschwollen.

(p. 614) Eine kolossale Vergrösserung weisen die Gaumen-drüsen auf. (Siehe Fig. C.)

Der Gaumen ist beiderseits bis über die Grenze des weichen Gaumens hinaus von je einer fast kastaniengrossen, scharfbegrenzten Geschwulst eingenommen. Beide Geschwülste reichen bis an den Alveolarrand, lassen aber in der Mittellinie eine $\frac{1}{2}$ cm breite, nach vorn allmählich breiter werdende Furche von normalem Aussehen frei. Nach vorn reichen sie bis an den I. Prä-molaris. Die Oberfläche der Anschwellungen erscheint glatt, die Schleimhaut darüber unverändert, die Konsistenz prall elastisch.

Unter der Wangenschleimhaut finden sich beiderseits vor dem Ausführungsgange der Ductus Stenonianus etwa erbsengrosse, bewegliche Knoten (accessorische Drüsen). Ausserdem liegen noch weiter vorn, gegen das Vestibulum oris zu, mehrere bis erbsengrosse, bewegliche Knötchen unter der Wangenschleimhaut.

Während der Untersuchung findet reichlich Speichelabsonderung statt, doch sind sonst keine Erscheinungen von Speichelfluss vorhanden. An der Mundschleimhaut keine auffällige Veränderung. Mehrere Zähne fehlen, einzelne sind cariös.

Da nur die Anschwellung der Thränendrüsen dem Kranken hinderlich war, wurde zunächst eine partielle Entfernung derselben, soweit sie das Oeffnen der Lidspalte erschwerten, vorgenommen (p. 615) (1. Februar 1888). Circa $1\frac{1}{2}$ cm langer, horizontaler Schnitt in der Verlängerung der Lidspalte, Spaltung der Konjunktiva über dem am meisten vorspringenden Teil des Tumors. Die Drüse wurde nun stumpf bis unter den Orbitalrand freipräpariert und der entblösste Teil mit der Schere abgetragen. Naht der Hautwunde. Es wurde auf jeder Seite eine etwa $2\frac{1}{2}$ cm lange, $1-1\frac{1}{2}$ cm im Durchmesser haltende Masse der Geschwulst, nach meiner Schätzung ungefähr $\frac{2}{3}$ des ganzen Tumors entfernt. Es folgte glatte Heilung. Schon nach wenigen Tagen

war der funktionelle Erfolg ein so evidenter, dass Pat. befriedigt die Klinik verlassen konnte.

Die Besserung des Zustandes hielt jedoch nicht lange an. Bald kamen die Geschwülste an den Augenlidern wieder zum Vorschein und verengerten die Lidspalten fast in demselben Masse als vor der Operation. Auch vergrösserten sich die Tumoren an den Kieferwinkeln zusehends. Aus diesem Grunde kam Pat. Ende März abermals in die Klinik. Sämmtliche Tumoren schienen um Geringes an Umfang zugenommen zu haben. Die Anschwellung der Thränendrüsen hat fast den alten Umfang wieder erreicht.— Es wird ein Versuch mit Pilokarpininjektionen gemacht, in der Hoffnung, durch vermehrte Sekretion eine Volumesabnahme der vergrösserten Drüsen zu erzielen. Trotz reichlicher Salivation ist ein Erfolg nicht zu konstatieren; deshalb wird nach 18 Tagen die Kur abgebrochen und auf dringendes Verlangen des Kranken abermals zum Messer gegriffen. Am 19. April wird unter gleicher Schnittführung wie das erste Mal die ganze Thränendrüse rechterseits exstirpiert. Die letzten tief gelegenen Reste werden mit dem scharfen Löffel hervorgeholt. Glatte Heilung. Am 1. Mai wird in gleicher Weise die Thränendrüse entfernt. Gleichzeitig werden auch beiderseits die vergrösserten Submaxillardrüsen exstirpiert. Sie liegen ebenso locker, wie die normale Drüse, in ihrem Lager, und lassen sich mühelos und unter geringfügiger Blutung ausschälen. Glatte Heilung per primam intentionem. Nach 10 Tagen wird Pat. entlassen.

Ueber das weitere Schicksal des Kranken liegen nur briefliche Berichte vor. Am 12. Juli, also 2 Monate nach seiner Entlassung, schrieb er mir selbst, er sei mit seinem Zustande sehr zufrieden. Die Anschwellung der Ohrspeicheldrüsen scheine allerdings noch zuzunehmen, sie hindere ihn aber nicht. Er sei im Gebrauche der Augen gar nicht behindert, obwohl er den ganzen Tag in der Sonnenhitze auf dem Felde arbeiten müsse. Die Anschwellungen am Halse (Submaxillardrüsen) seien nicht wieder gekommen. Er fühle sich auch sonst ganz gesund.

(p. 616) Am 25. Juli erkrankte er plötzlich unter den Erscheinungen einer Peritonitis (Perityphlitis?), nachdem er noch Tags vorher seiner Arbeit nachgegangen war. Er erlag der Krankheit

am 9. Tage. Die Geschwülste in der Parotisgegend und im Munde sollen sich während dieser Erkrankung binnen wenigen Tagen rapid zurückgebildet haben, so dass sie vor dem Tode fast verschwunden waren.

Ueber die anatomische Untersuchung der exstirpierten Teile kann ich folgendes berichten. Am meisten Beachtung verdient die Untersuchung der Submaxillardrüsen, welche in toto entfernt worden sind. Zunächst muss hervorgehoben werden, dass jede der auf Kinderfaustgrösse angeschwellenen Drüsen in Bezug auf Form und Gliederung in Lappen und Läppchen genau den Verhältnissen der normalen Drüse entsprach. Die Totalansicht und der Querschnitt des Tumors, auf Taf. IX Fig. 1 und 2 dargestellt, geben ein treues Bild davon. Der Tumor zeigte in den gröberen makroskopischen Einzelheiten den normalen Bau der Drüse, nur in's Masslose vergrössert. Ein wesentlicher Unterschied fand sich jedoch auf dem frischen Querschnitt schon für das blosse Auge in der Farbe und im feineren Gefüge der die einzelnen Läppchen bildenden Drüsenmasse. An Stelle des feinkörnigen, graurötlichen Gefüges der normalen Drüsensubstanz sehen wir eine mehr homogene, blassrötlichgelbe, speckige Masse von leichter Transparenz. Die Konsistenz ist vermindert, speckig. Die Zahl der Blutgefässe scheint nur in den Septis, der Grössenzunahme des Organs entsprechend, vermehrt zu sein; die Drüsensubstanz selbst erscheint auffallend gefässarm.

Die mikroskopische Untersuchung ergab, dass die Hauptmasse des Tumors aus einem ziemlich gleichmässig angeordneten Gewebe kleiner Rundzellen bestand. (Siehe Tafel IX, Fig. 3.) Die Zellen liegen stellenweise dichter beisammen; an anderen Stellen ist zwischen ihnen ein feines Retikulum zu erkennen. Vereinzelte, grössere Zellen lassen deutlich Kernteilungsfiguren erkennen. In diese kleinzellige Hauptmasse eingebettet erscheinen, teils einzeln, teils gruppenweise, die anscheinend unveränderten Acini der Speicheldrüse. Sie sind durch das Rundzellengewebe gewissermassen auseinander gedrängt, auseinander geworfen.

Aehnliche Verhältnisse boten sich bei der mikroskopischen

Untersuchung der Thränendrüse dar; nur dass hier die Acini weit seltener anzutreffen waren und, wie es scheint, in den am meisten nach aussen gedrängten Partien der Geschwulst ganz fehlten.

(p. 617) Versuchen wir den beschriebenen Fall zu deuten, so stossen wir auf mannigfache Schwierigkeiten. Der Krankheitsprozess stellt sich klinisch als eine langsam entstehende, kolossale Vergrösserung sämtlicher Speichel- und Thränendrüsen dar, ohne entzündliche Erscheinungen, ohne nachweisbare Mitbeteiligung des Gesamtorganismus. Der Prozess bleibt auf das Gebiet dieser Drüsen scharf beschränkt, er zieht weder die Nachbarschaft, noch andere Organe und Gewebe in Mitleidenschaft. Die mikroskopische Untersuchung ergibt, dass das eigentliche Drüsenparenchym dabei eine ganz passive Rolle spielt. Die Grössenzunahme ist lediglich durch eine massenhafte, kleinzellige Infiltration des interstitiellen Bindegewebes bedingt.

Es ist klar, dass der mikroskopische Befund allein hier den Prozess nicht erklären kann. Wäre eine einzige Drüse in der geschilderten Weise verändert, so würden wir nicht anstehen, an eine echte Geschwulst zu denken. Wissen wir doch, dass gerade in den Speicheldrüsen, vom interstitiellen Bindegewebe ausgehend, die mannigfachsten Geschwülste aus der Bindegewebsreihe, zumal auch Rundzellensarkome, vorkommen. Einem typischen Rundzellensarkom entspricht aber hier schon der histologische Befund nicht; ausserdem widerspricht das makroskopische und noch mehr das klinische Verhalten dem Bilde des echten Sarkoms. Ich meine die strenge Respektierung der Grenzen der Drüse und ganz besonders der grösseren und kleineren Septa zwischen den Drüsenläppchen. Die histologische Beschaffenheit der kleinzelligen Infiltration entspricht am ehesten dem Verhalten lymphadenoiden Gewebes. Demnach könnte man histologisch an ein Lymphom oder Lymphosarkom denken.¹ Hiermit begeben wir uns aber auf einen unsicheren Boden, auf ein Gebiet, in welchem

¹ Ich habe nach der ersten mikroskopischen Untersuchung den Prozess in der That als Lymphosarkom aufgefasst und in diesem Sinne auch Herrn Prof. Fuchs in Wien von dem Falle Mitteilung gemacht.

klinische Beobachtung und histologische Forschung noch nicht völlig in Einklang gebracht sind und auf welchem die Nomenclatur noch recht unklar und zweideutig ist. Wir könnten zunächst an jene Formen von Geschwülsten denken, welche primär von Lymphdrüsen oder von präformiertem lymphadenoiden Gewebe ausgehen und als maligne Lymphome (Pseudoleukaemie) bezeichnet werden. Heidenhain¹ hat im interstitiellen Bindegewebe der Speicheldrüsen, namentlich in der Sublingualis lymphatisches Gewebe nachgewiesen; gegen die Annahme einer primären Lymphombildung in der Speicheldrüse (p. 618) ist daher a priori nichts einzuwenden. Das vollständige Fehlen einer Mitbeteiligung der Lymphdrüsen und der Milz—wie sie z. B. auch die sog. Pseudoleukämie der Haut begleitet—spricht jedoch gegen den Charakter maligner Lymphome.

Aber auch die Annahme eines Lymphosarkoms, wie es ausser den Lymphdrüsen gelegentlich im Hoden und in anderen Organen vorkommt, ist nach meiner Meinung nicht zulässig. So weit mir die Fälle dieser Art bekannt sind, handelt es sich immer um maligne Neubildungen, die früher oder später Metastasen machen. Der klinische Verlauf entspricht dem des typischen Sarkoms. In unserem Falle war der klinische Verlauf während der 14 monatlichen Beobachtung trotz des Recidivs von Seiten der Thränenrüsen kein maligner; in den letzten Lebenstagen des Kranken bildeten sich die nicht operierten Tumoren rapid zurück. Ueberlegen wir ferner, dass das fast gleichzeitige Auftreten zahlreicher Erkrankungsherde an örtlich völlig getrennten Stellen unseren Erfahrungen über bösartige Geschwülste direkt widerspricht, so müssen wir die Annahme einer solchen in unserem Falle entschieden zurückweisen.

Das Resultat unserer Betrachtung ist somit ein rein negatives. Ueber die Bedeutung des Prozesses kann ich nur Vermutungen aussprechen. Bevor ich aber die Gedanken ausspreche, die ich mir in der Richtung gemacht habe, möchte ich die Fälle anderer Beobachter anführen, soweit sie zu dem meinigen in Beziehung zu bringen sind.

¹ Studien des physiologischen Institutes zu Breslau 1868, 4. Heft, S. 116.

Die meiste Aehnlichkeit mit meinem Falle hat ein vor kurzem von Fuchs¹ mitgeteilter, in welchem beiderseits die Thränendrüsen und Parotiden erkrankt waren. Ferner ein vor 3 Jahren mitgeteilter Fall von Haltenhoff² mit gleichzeitiger Anschwellung der Thränendrüsen, der Parotiden und Submaxillardrüsen beider Seiten.

Der Fall von Fuchs ist folgender:

61jähriger, kräftiger Mann, von Beruf Glaser. Er bemerkte vor 5 Monaten eine Anschwellung der oberen Augenlider, vor 4 Wochen die Geschwulst in der Parotisgegend. Vorstellung in der Klinik des Prof. Fuchs in Wien im März 1890. Die beiden oberen Augenlider in ihrer äusseren Hälfte durch eine Geschwulst vorgetrieben, die im äusseren oberen Teil der Orbita lag. Der vordere Rand der Geschwulst fühlte sich hart und höckerig an; die Lider selbst waren darüber verschieblich. Wurde das Lid stark in die Höhe gezogen, so erschien die Uebergangsfalte (p. 619) in ihrer äusseren Hälfte durch eine braunrote Geschwulst vorgewölbt. Die Bulbi etwas vorgetrieben, im übrigen intakt. Sehvermögen ungestört.—Anschwellung beider Ohrspeicheldrüsen; sie stellte sich als eine abgeplattete Geschwulst von 4–5 cm Durchmesser dar, die auf dem aufsteigenden Unterkieferaste lag und sich so weit nach hinten erstreckte, dass das Ohrläppchen abgezogen erschien. Konsistenz hart, Oberfläche leicht höckerig. Die übrigen Speicheldrüsen, sowie die Lymphdrüsen waren intakt, ebenso die Hoden. Innere Organe und Blut normal. Syphilis nicht vorhanden.

Pat. bekam in täglich steigender Dosis *Solutio arsenicalis* Fowleri. Er kam aber nur bis 14 Tropfen, weil er einen akuten Ausschlag bekam. Nach 2 Monaten war die Thränendrüsengeschwulst der rechten Seite deutlich verkleinert, während sie auf der linken unverändert blieb. Auch die Parotischgeschwülste, namentlich die rechte, waren erheblich kleiner geworden. Ein zweiter Versuch der Arsenikkur musste abermals abgebrochen werden, weil Pat. unter Schüttelfrost einen Ausschlag bekam und abmagerte. Im Mai 1891, also 14 Monate nach der ersten Vorstellung, konstatierte Fuchs ungefähr denselben Befund wie das erste Mal. Sämtliche Anschwellungen waren wieder ungefähr zur ursprünglichen Grösse herangewachsen. Sie waren aber auch jetzt indolent,

¹ Gleichzeitige Erkrankung der Thränendrüsen und der Parotiden. Beiträge zur Augenheilkunde. Heft III, 1891.

² Hyperplasie lymphatique des glandes lacrymales et salivaires. Annales d'oculistique 1889.

hart, nirgends mit der Umgebung verwachsen, so dass sie ganz frei beweglich erschienen. Das Allgemeinbefinden war gut.—Bei der ersten Vorstellung des Kranken excidierte Fuchs ein kleines Stückchen von demjenigen Teil der Thränendrüse, der sich am meisten unter der oberen Uebergangsfalte hervordrängte. Bei der Untersuchung dieses Stückchens fanden sich, in das kaum veränderte submuköse Gewebe der oberen Uebergangsfalte eingebettet, grössere und kleinere Knoten, welche den Bau von Lymphomen zeigten. Die meisten waren gegen das umgebende Gewebe scharf abgegrenzt; sie bestanden aus dicht gedrängten, einkernigen Zellen, deren Kerne rund oder ein wenig oval, stark granuliert und mit den angewendeten Färbemitteln intensiv gefärbt waren. An manchen Kernen erkannte man das sehr spärliche, siegelringartig angeordnete Zellprotoplasma; an den meisten Kernen war aber eine deutliche Protoplasmahülle nicht zu erkennen. Zwischen den zelligen Elementen befand sich kein deutliches Reticulum, sondern eine fast homogene Zwischensubstanz. Einzelne dünnwandige Blutgefässe fanden sich im Inneren der Knoten; nirgends eine Spur von Zerfall, noch von epitheloïden oder Riesenzellen. Elemente der Drüse wurden nicht gefunden.

Die Krankengeschichte des Falles von Haltenhoff ist in Kürze folgende.

12jähriges Mädchen, früher wegen phlyktenulärer Conjunctivitis in der Augenklinik behandelt. Vor 4 Monaten entwickelte sich allmählich, ohne bekannte Ursache, ohne Fieber, ohne Beschwerden eine Anschwellung der oberen Augenlider, vor den Ohren und unter den Kieferwinkeln, u. z. zuerst am rechten, dann am linken Auge und dann an den anderen Stellen.—Gut entwickeltes Kind, von etwas blassem Aussehen, sonst gesund. Symmetrische Vorwölbung der äusseren Hälfte der oberen Augenlider durch eine unter der Lidhaut sitzende, unbewegliche Geschwulst; keine Rötung, kein Oedem, keine Gefäss-Ektasieen. Die Haut über dem Tumor verschiebbar; der Tumor selbst glatt, hart, völlig schmerzlos; er entspricht der Lage nach der Thränendrüse. Wird das obere Augenlid umgestülpt, so erscheint die Uebergangsfalte durch einen rötlichen Tumor hervorgedrängt. Conjunctiva am Bulbus im übrigen intakt. Beide Parotiden in ihrer ganzen Ausdehnung zu indolenten, fast brettharten Tumoren angeschwollen, (p. 620) die dem Kinde ein, dem Bilde des Mumps ähnliches, Aussehen geben. Auch die Submaxillardrüsen sind in symmetrische Geschwülste

von ähnlicher Beschaffenheit umgewandelt. An den Sublingualdrüsen keine Veränderung nachweisbar. Keinerlei Lymphdrüsenanschwellungen. Innere Organe gesund. Mandeln etwas vergrößert, die Pharynxschleimhaut etwas geschwollen. Die Zähne intakt, die Gingiva und Mundschleimhaut von normalem Aussehen. Nach Angabe der Mutter soll das Kind öfter husten und sich schnäuzen; der Nasenschleim sei öfter übelriechend. Zur Zeit besteht ein geringfügiges Eczem am Naseneingang.—Speichel- und Thränenabsonderung nicht vermehrt. Hämoglobingehalt des Blutes (nach Gowers) 85%. Der Patientin wird ausser roborierender Diät und Bewegung in frischer Luft Jodeisensyrup verordnet. Schon nach 14 Tagen ist eine Volumsabnahme an den Geschwülsten bemerkbar. Nach mehr als einem Jahre war das Mädchen von blühendem Aussehen. Die Submaxillardrüsen sind nicht mehr zu fühlen, dagegen erscheinen die Parotiden noch etwas stärker als normal. Die Thränendrüsen fühlt man gerade noch dicht am Orbitalrand.

Ich habe die zwei Fälle von Fuchs und Haltenhoff ausführlicher wiedergegeben, weil sie für die Charakteristik des vorliegenden Krankheitsprozesses von Bedeutung sind. Wenn auch im Fall von Haltenhoff kein histologischer Befund vorliegt, so stimmt er doch klinisch mit den anderen zweien so völlig überein, dass wir annehmen dürfen, es handle sich in allen drei Fällen um denselben Prozess. Der Fall von Haltenhoff ist insofern besonders wichtig, weil hier innerhalb Jahresfrist die fast vollständige Rückbildung der Geschwülste konstatiert wurde.

Ausser den angeführten finde ich noch zwei Fälle in der Literatur, die höchst wahrscheinlich auch hierher gehören.¹ Den einen Fall von Reymond² kenne ich nur nach einem Referat: Bei einem 57 jährigen Mann bestand seit 2–3 Jahren beiderseits eine Anschwellung an den oberen Augenlidern, in der Parotisgegend und an den Achseldrüsen. Die Geschwulst der Orbita wurde exstirpiert; die mikroskopische Untersuchung erwies lymphoïdes Gewebe, das an einzelnen Stellen Zeichen amyloider Degeneration erkennen liess. Der zweite Fall wurde als Sarkom der

¹ Nachträglich teilt mir Herr Professor Fuchs mit, dass er in der letzten Zeit noch zwei andere dem ersten analoge Fälle, nur leichter Art beobachtet habe. Die Anschwellungen nahmen nach Monaten unter Arsengebrauch ab. Leukämie war in keinem der Fälle vorhanden.

² Arch. d'ophthalmologie VI, 23.

Thränendrüsen im Jahre 1889 von Adler in der Gesellschaft der Aerzte zu Wien vorgestellt.¹

Ich teile die Krankengeschichte im Auszug mit.

70jähriger Mann, hat ausser Pneumonie und Dysenterie keine Krankheiten durchgemacht, war auch nicht syphilitisch. Vor einem Jahre bemerkte er beiderseits (p. 621) in der Gegend der Thränendrüse das Auftreten von Geschwülsten, die allmählich bis zur jetzigen Grösse wuchsen. Befund am 3. April 1889: Am oberen äusseren Rande beider Augenhöhlen ziemlich symmetrisch stehen circa $3\frac{1}{2}$ cm lange, 16 mm breite Geschwülste; der rechtsseitigen sitzt noch ein erbsengrosser Höcker auf. Der Rand der Geschwulst setzt sich mehr nach aussen und abwärts ins Lid fort. Die Geschwülste sind knorpelhart, von höckeriger Oberfläche, nicht schmerzhaft; sie lassen sich unter der Lidhaut, jedoch nicht gegen den Orbitalrand verschieben und sitzen an der Orbitalwand fest. Die Lidspalten in allen Dimensionen verengert, von zeckiger Form mit der Spitze nach oben. Im äusseren Abschnitt des linken oberen Augenlides Ektropium. Beim Umstülpen des Oberlides bemerkt man, dass die Conjunctiva im Bereich der Uebergangsfalte degeneriert und teils von Wucherungen in der Grösse von Trachomkörnern, teils von hahnenkammartigen Excrescenzen besetzt ist. Conjunctiva bulbi et tarsi normal. Seit 3 Monaten bemerkt Pat. ausserdem verschiedene Drüsenanschwellungen. Zur Zeit sind zu harten Knollen angeschwollen die Cervical-, Praeauricular- und Submaxillardrüsen. Seit 6 Wochen Heiserkeit, seit 3 Wochen eine „Hervorragung“ am harten und weichen Gaumen. Im Rachenraume eine so bedeutende Schwellung, dass die laryngoskopische Untersuchung unmöglich ist. Die Untersuchung eines exstirpierten Teiles der Conjunctiva ergab ein „kleinzelliges Sarkom.“ Es wurde angenommen, dass ein primäres Sarkom der Thränendrüsen vorliege mit allgemeiner Sarkomatose. Aus diesem Grunde wurde von jedem operativen Eingriff abgesehen und eine Arsenkur eingeleitet (Tinct. Fowleri bis 10 Tropfen täglich). Nach 6 Wochen trat eine sichtliche Besserung ein. Die Heiserkeit verschwand, die Schwellung am Gaumen nahm ab, die Geschwülste der Thränendrüsen verkleinerten sich zusehends, so dass sie nur mehr 2 cm lang und 11 mm breit waren. Die mikroskopische Untersuchung eines abermals excidierten Stückchens der erkrankten Conjunctiva bestätigte die frühere histologische Diagnose; es wurde aber nun, mit Rück-

¹ Sitzung vom 17. Mai 1889. Siehe Wiener klinische Wochenschrift 1889, S. 422.

sicht auf den Erfolg der Arsenbehandlung, ein Lymphosarkom resp. malignes Lymphom angenommen. Mitte September 1892, also fast 4½ Jahre nach Beginn der Erkrankung, ist der Kranke einer brieflichen Mitteilung des Herrn Primararzt Dr. Adler zufolge vollkommen geheilt. Er nimmt noch Arsen.

Die beiden Fälle von Reymond und Adler unterscheiden sich von den früheren wesentlich durch die Mitbeteiligung der Lymphdrüsen. Es kann daher die Frage entstehen, ob diese Fälle überhaupt hierher gehören; ein Zweifel in dieser Richtung scheint um so eher berechtigt, als die Erkrankung der Speicheldrüsen bei Reymond und Adler ganz in den Hintergrund tritt. Fuchs zweifelt überhaupt daran, dass im Falle von Reymond die Parotiden miterkrankt gewesen seien; er glaubt, dass die Lymphdrüsen der Präauriculargegend einen Parotistumor vorgetäuscht hätten. In dem Falle von Adler wird der Speicheldrüsen gar nicht Erwähnung gethan; gleichwohl können mässige Anschwellungen unter den intumescierten Präauricular- und Submaxillardrüsen der Beobachtung entgangen sein. Ich möchte an diese Möglichkeit denken, weil im Adler'schen Falle eine Gruppe von Drüsen, die zum Typus der Speicheldrüsen gehören, sicher (p. 622) intumesciert waren. Ich meine die Gaumendrüsen. Die am harten und weichen Gaumen bestehende „Hervorragung“ kann ich wenigstens nur so deuten; sie entspricht auch dem Verhalten der Gaumendrüsen in meinem Falle.

Eine auffallende Aehnlichkeit mit den früheren haben die zwei Fälle in Betreff der Erkrankung der Thränendrüsen. Der klinische Verlauf, namentlich die Gutartigkeit des Prozesses, die symmetrische Entwicklung stimmen völlig überein. Auch der histologische Befund widerspricht nicht der Annahme eines gleichartigen Prozesses.

Die Erkrankung der Thränendrüsen ist in unseren Fällen nicht nur die konstanteste Erscheinung; sie ist auch diejenige, welche zuerst auftritt. Wir finden in den Krankengeschichten die zweifelloso Angabe, dass zuerst die Thränendrüsen anschwellen und später erst in wechselnder Reihenfolge die anderen Anschwellungen auftraten. Es scheint also, dass die Thränendrüsen den ersten und vornehmlichsten Angriffspunkt des Krankheitserregers

abgeben. Es wäre daher a priori auch die Möglichkeit einer isolierten Erkrankung der Thränendrüsen zuzugeben. Wir finden nun in der Litteratur in der That mehrere Fälle von Erkrankung der Thänendrüsen allein verzeichnet, welche nach meiner Meinung hierherzuzählen sind. Ich sehe von den in den Lehrbüchern häufig wiederkehrenden Angaben von „Hypertrophieen“ der Thränendrüsen ab; ebenso von mehrfachen kasuistischen Mitteilungen, die nur eine unsichere Deutung zulassen. Von den mir zugänglichen Fällen möchte ich nur drei anführen. Vor allem den genau beobachteten Fall von Arnold und Becker¹ aus dem Jahre 1872.

33 jähriger Müller, hereditär nicht belastet, bis zum 19. Lebensjahre gesund. Im 20. Lebensjahre wurde er von einer Entzündung beider Augen befallen, die er auf die Einwirkung des Staubes in der Mühle zurückführt. Die Augenentzündung hielt bis zum heutigen Tage in wechselnder Intensität an und veranlasste ihn wiederholt, ärztliche Hilfe zu suchen. Seit dem 30. Lebensjahr soll der Exophthalmus bestehen. 1. Februar 1871 Aufnahme in die Heidelberger Augen-klinik. Beide Augen waren stark aus der Orbita hervorgetrieben, ihre Achsen convergierten nach unten, ihre Beweglichkeit jedoch nach keiner Seite ganz aufgehoben. Das obere Augenlid war an beiden Augen stark ausgedehnt und konnte so gut wie gar nicht gehoben werden. Conjunctiva in der ganzen Ausdehnung gleichmässig gerötet, stark secernierend; am unteren Rande der rechten Cornea Gefässentwicklung. Starke Lichtscheu. Beträchtliche spontane Schmerzen waren nicht vorhanden. Als Grund des Exophthalmus liess sich in beiden Augenhöhlen eine im oberen äusseren Winkel derselben gelegene, rundliche, mehr als taubeneigrosse, (p. 623) derbe, nicht pulsierende und bei Druck nicht schmerzhaft Geschwulst mit glatter Oberfläche erkennen. Die Geschwulst hinter dem rechten Auge war beträchtlich grösser als die linke. Ein Zusammenhang mit dem Bulbus bestand nicht.—Es wurde eine Hypertrophie der Thränendrüsen angenommen und die Exstirpation beider Tumoren durch einen parallel mit dem oberen Orbitalrande geführten Schnitt ausgeführt. Anfangs Juni 1872 haben beide Bulbi normale Lage und Beweglichkeit. Der Tumor ist nicht recidiviert. Die Conjunctiva an beiden Augen ist sammetartig aufgelockert und leicht injiciert, die Conjunctiva bulbi netzförmig injiciert. Keine Spur

¹ Doppelseitiges, symmetrisch gelegenes, Lymphadenom der Orbita, Gräfe's Archiv. XVIII, 2. Abt. 56.

von Trachomkörnern. Vermehrte Sekretion. Sehschärfe normal.— Am 9. November 1872, also $1\frac{3}{4}$ Jahre nach der Operation, sind die Tumoren nicht recidiviert.

Die von Prof. Arnold vorgenommene Untersuchung ergibt, dass sich der Tumor im wesentlichen aus lymphatischem Gewebe zusammensetzt. Dichte Anhäufungen lymphoider Elemente, welche in ein zartes Reticulum eingebettet und gegen die Nachbarschaft scharf abgegrenzt erscheinen, ahmen vollständig den Typus von Lymphfollikeln nach. Sie liegen in einem mehr gleichartig angeordneten, diffusen lymphatischen Gewebe. Stellenweise finden sich stärkere Bindegewebszüge. Arnold nimmt keinen Anstand, die Geschwülste als eigentliche Lymphadenome, d. i. Neubildung lymphatischen Gewebes, zu deuten. In Bezug auf den Ausgangspunkt derselben spricht er nur Vermutungen aus. Zur Annahme einer echten Heteroplasie, der Entwicklung lymphatischen Gewebes aus dem Bindegewebe der Orbita, kann er sich nur schwer entschliessen. Viel wahrscheinlicher erscheint es ihm, dass an der betreffenden Stelle im Bindegewebe der Orbita normalerweise oder bei einzelnen Individuen präformiertes, lymphatisches Gewebe liege, das hier den Ausgangspunkt der Geschwulst abgegeben habe. Dies sei aber nur Hypothese, da der thatsächliche Nachweis eines derartigen präformierten Gewebes zur Zeit fehle.

Nur sehr spärliche Aufzeichnungen konnte ich leider über die anderen zwei Fälle finden. Der eine wurde mit wenigen Zeilen von Korn¹ im Jahre 1869 mitgeteilt, und zwar unter Bezugnahme auf einen von Horner publicierten Fall von beiderseitiger, akuter Thränendrüseneentzündung. Der Fall betrifft eine Cigarrenarbeiterin, die seit 4 Monaten an einer Anschwellung der Thränendrüsen litt. Aus der der Mitteilung beigegebenen Abbildung geht hervor, dass es sich um eine symmetrische, in der Thränendrüsengegend gelegene Geschwulst handelte, welche genau so, wie in den anderen Fällen, die äussere Hälfte der Uebergangsfalte weit nach unten drängte.

Den anderen Fall von Power² kenne ich nur aus Referaten.

¹ Klinische Monatsblätter für Augenheilkunde. 1868, VII, 181.

² Transaction of the ophthalm. 1867, p. 109.

(p. 624) Ein 14 jähriger, im übrigen gesunder Knabe litt seit einem halben Jahre an einer Anschwellung beider Thränendrüsen. Nachdem Medikamente erfolglos blieben, wurde die linke Thränendrüse exstirpiert. Die mikroskopische Untersuchung ergab eine Hypertrophie des interstitiellen Gewebes, während sich an der Drüsensubstanz keine auffälligen Veränderungen fanden.

Die mangelhaften Daten über die zwei zuletzt angeführten Fälle gestatten sicher nicht, dieselben ohne Weiteres mit dem Beckerschen in eine Parallele zu stellen und damit unseren früheren Fällen anzureihen. Immerhin gehören sie insofern hierher, als es sich um eine chronische, symmetrisch auftretende Geschwulstbildung im Bereich der Thränendrüsen mit gutartigem Charakter handelt. Dagegen stehe ich nicht an, den Becker'schen Fall trotz der isolierten Erkrankung der Thränendrüsen den früheren direkt an die Seite zu stellen.

Während wir demnach Beobachtungen über eine isolierte Erkrankung der Thränendrüsen nach dem beschriebenen Typus verzeichnet finden, suchen wir vergebens nach ähnlichen Beobachtungen, die sich auf die Speicheldrüsen allein unter Ausschluss der Thränendrüsen beziehen. Weder in den Lehrbüchern, noch in den einschlägigen Monographien finden wir diese Affektion angedeutet. Die grundlegende Arbeit von Billroth¹ über die Speicheldrüsengeschwülste, die spätere ausgezeichnete Arbeit von Kaufmann² über die Parotis-Sarkome und eine jüngst erschienene Arbeit von Nasse³ enthalten keine einzige Beobachtung, welche hieher zu beziehen wäre. Es muss auch auffallen, dass mit Ausnahme meines Falles alle hier angeführten Beobachtungen von Ophthalmologen herrühren.

Ich möchte es nicht unterlassen, hier auch noch einige andere Beobachtungen anzuführen, welche sich auf die gleichzeitigen Erkrankungen der Thränen- und Speicheldrüsen resp. Lymphdrüsen beziehen, aber ausser dieser einen Aehnlichkeit mit unseren Fällen wenig gemein haben. Zunächst ein von Gordon Norrie⁴ mit-

¹ Beobachtungen über Geschwülste der Speicheldrüsen. Virchow's Archiv XVII, 357.

² Das Parotis-Sarkom. Arch. f. klin. Chir. XXVI, 672.

³ Die Geschwülste der Speicheldrüsen und verwandte Tumoren des Kopfes. Arch. f. klin. Chir. XXXIV, 233.

⁴ Centralblatt f. Augenheilk. 1890, 223.

geteilter Fall von akuter Entzündung beider Thränendrüsen im Gefolge einer epidemischen Parotitis bei einem 11 jährigen Mädchen, den der Autor wohl mit Recht als echten Mumps der (p. 625) Thränendrüse auffasst. Dann berichtet Galezowski¹ über einen Fall von akuter Entzündung der Thränendrüsen, welchen er bei einer 40 jährigen Frau beobachtete; die Erkrankung war von einer Schwellung der Präauricular- und Submaxillar-Lymphdrüsen begleitet. Ferner teilt Scheffels² einen Fall von doppelseitiger, nicht eitriger, fieberlos verlaufender Dakryoadenitis mit. Die Affektion war nicht schmerzhaft. Gleichzeitig waren auch die submaxillaren Speichel- und Lymphdrüsen zu kinderfaustgrossen Tumoren angeschwollen; ausserdem fanden sich noch anderwärts Lymphdrüsenschwellungen und eine Vergrösserung der Milz. Parotis und Präauriculardrüsen waren unverändert. Binnen 13 Tagen gingen die Anschwellungen nach Jodkaliumgebrauch zurück. Einen Fall von akuter, indolenter und ohne Fieber verlaufender Anschwellung beider Thränendrüsen teilt auch Horner³ mit. Auch hier ging nach Jodkaliumgebrauch binnen 3 Wochen die Anschwellung zurück. Doch fehlten begleitende Erscheinungen von seiten der Speichel- und Lymphdrüsen.

Von chronischen Prozessen, welche mit der uns beschäftigenden Affektion eine gewisse Aehnlichkeit haben, kommen meines Wissens nur die leukämische Anschwellung und die Tuberkulose der Thränendrüse in Begleitung der gleichnamigen Affektion der Lymphdrüsen vor.

Einen Fall von Leukämie dieser Art hat Gallasch⁴ beschrieben. Er betrifft ein 4½ jähriges Mädchen, das an typischer Leukämie litt und diesem Leiden auch erlag. Ausser der Anschwellung der Milz, Leber und der Lymphdrüsen verschiedener Regionen waren auch die Thränendrüsen, die Parotiden und die Sublingualdrüsen intumesciert. Gallasch fand die Thränendrüsen in gleicher Weise

¹ Recueil d'ophthalmologie 1886, 415.

² Centralbl. f. Augenheilk. 1890, 136.

³ Klinische Monatsblätter 1866, IV, 257.

⁴ Beiderseitige leukämische Infiltration der Thränendrüse. Jahrb. für Kinderheilkunde. 1874, VII 1, Seite 82.

wie die anderen erkrankten, drüsigen Organe in einem leukämischen Tumor aufgegangen.

Fälle dieser Art scheinen sehr selten zu sein, wenigstens finde ich keine anderweitige Beobachtung in der Litteratur. Gewiss ebenso selten dürfte eine tuberkulöse Infiltration der Thränen-drüsen sein. Ich habe einen charakteristischen Fall dieser Art in Königsberg beobachtet. Die Erkrankung beider Thränen-drüsen schloss sich an die Entwicklung zahlreicher tuberkulöser Lymphome der Parotis- und Submaxillargegend (p. 626) an. Ich teile den Fall seiner Seltenheit wegen ausführlich mit.

Eduard Stein, 20 Jahre alt, Müller aus Rogehnen in Ostpreussen. Der Vater ist lungenleidend, die Mutter und 3 Brüder gesund. Der bis dahin stets gesunde, junge Mann bemerkte vor einem Jahre das Auftreten eines etwa haselnussgrossen Knotens unter dem Kinn. Bald kamen neue Knoten in der Nachbarschaft hinzu; sie wuchsen innerhalb weniger Wochen verhältnismässig rasch, nahmen aber dann nur ganz unmerklich an Umfang zu. So entwickelten sich im Verlaufe von 8–10 Monaten nach und nach die jetzt vorhandenen Anschwellungen am Gesicht und Hals. Erst vor 4 Wochen bemerkte Pat. die Entwicklung der Geschwulst im linken oberen Augenlid. Beschwerden hatte er nie davon.—Seit einiger Zeit leidet er an Husten.—Befund am 2. Mai 1889. Kräftig gebauter, gut genährter Mann von sonst gesundem Aussehen. Beide Submaxillarregionen sind von zusammenhängenden Paketen bohnen- bis über haselnussgrosser Drüsen eingenommen. (Siehe beistehende Figur D.) Die einzelnen (p. 627) Drüsen sind glatt, von derber Konsistenz; sie lassen sich sowohl gegen einander, als auch in toto auf der Unterlage in mässigen Grenzen verschieben. Die Haut darüber unverändert, verschiebbar. Das linksseitige Drüsenpaket ist umfangreicher als das rechte und geht ohne Unterbrechung in eine zweite Gruppe teils zusammenhängender, teils isolierter Drüsen in der Masseter- und Parotisgegend über. Die bohnen- bis kirschgrossen Drüsen reichen bis an den Processus zygomaticus und liegen vorwiegend auf der Fascia parotideo-masseterica. Die Praeauriculardrüsen sind auf Bohnengrösse geschwollen. Eine kleinere Gruppe von Drüsen findet sich in der rechten Parotisgegend. Ein weiterer, zusammenhängender Zug von ebenso grossen Drüsen geht längs des vorderen und hinteren Randes des Kopfnickers der linken Seite bis an die Clavicula herunter. Die einzelnen Drüsen haben hier überall dieselbe Beschaffenheit, wie die zuerst beschriebenen. Ferner finden sich in mässigem Grade gesch-

wollen und verhärtet die Submental-, Cervical-, Axillar-, Cubital- und Inguinaldrüsen.—

Die äusseren 2 Drittel des linken oberen Augenlides sind stark vorgewölbt und verbreitert. Dem entsprechend erscheint der betreffende



Fig. D

Abschnitt des Lidrandes tiefer gestellt, die Lidspalte verengert. Der tastende Finger findet unter der sonst unveränderten Lidhaut eine circa 2 cm lange, walzenförmige Geschwulst von glatter Oberfläche und prall elastischer Konsistenz. Die Geschwulst lässt sich allenthalben bis an

den Orbitalrand verfolgen und scheint der oberen Orbitalwand fest aufzusitzen. An Conjunctiva und Bulbus keine nachweisbaren Veränderungen. Durch Palpation kann man auch an der analogen Stelle des rechten oberen Orbitalrandes eine flache, derbe, der Orbitalwand aufsitzende Geschwulst nachweisen, die mit ihrer vorderen Kante gerade den Orbitalrand erreicht.—Milzdämpfung etwas vergrößert, doch ist die Milz nicht zu tasten. Im übrigen in den inneren Organen keine nachweisbaren Veränderungen. Keine Vermehrung der Leukocyten.—

Es wird zunächst in der Annahme, dass maligne Lymphome vorliegen, ein Versuch mit der Arseniktherapie (innerlich) gemacht. Da Pat. trotz ganz allmählicher Steigerung grössere Dosen nicht verträgt, wird seinem Wunsche gemäss nur die Geschwulst am linken Auge entfernt. 1 cm langer Horizontalschnitt in der Verlängerung der Lidspalte, Durchtrennung der Conjunctiva über dem Tumor, Ausschälung der ganzen Thränendrüse mit Pincette und Schere. Naht bis auf den sussersten Wundwinkel, durch welchen ein schmaler Jodoformgaze-streifen in die Wundhöhle gelegt wird. Heilung unter geringfügiger Eiterung.—

Die Hauptmasse der wohl auf das 10 fache vergrößerten Thränendrüse besteht aus Granulationsgewebe; in diesen finden sich zahlreiche typische Tuberkel mit Langhans'schen Riesenzellen.

Vielleicht ist auch ein von Frost¹ mitgeteilter Fall als Tuberkulose der Thränendrüse aufzufassen. Die Anschwellung derselben war im Verlaufe von 9 Monaten zu Stande gekommen. Die mikroskopische Untersuchung der exstirpierten Drüse ergab, dass die Geschwulst im wesentlichen aus einem granulationsähnlichen, kleinzelligen Gewebe bestand, das die eigentliche Drüsensubstanz grösstenteils zum Schwund gebracht hatte. An einzelnen Stellen fanden sich regressive Veränderungen, an zwei Stellen Verkäsung.

(p. 628) Die zuletzt angeführten Fälle von akuten und chronischen Erkrankungen der Thränendrüsen sind für uns deshalb wichtig, weil sie darthun, dass 1) eine beiderseitige Beteiligung der Thränendrüsen bei verschiedenartigen Affektionen vorkommt, somit für die uns interessierende Krankheit allein nicht charakteristisch ist, 2) dass auch bei anderen akuten und chronischen Erkrankungen eine gewisse Wechselbeziehung sowohl zwischen

¹ Transaction of the ophthalm. 1887, 109.

Thränen- und Speicheldrüsen, als auch zwischen den Thränen und den benachbarten Lymphdrüsen besteht. Wodurch diese Wechselbeziehungen begründet sind, darüber kann man nur Vermutungen aussprechen. Vielleicht sind sie dadurch gegeben, dass sowohl in der Thränendrüse als auch in der Speicheldrüse, d. i. in dem sie umgebenden und durchsetzenden Bindegewebe, normalerweise kleinste lymphatische Elemente vorkommen. Damit ist die Bildung pathologischen, lymphoiden Gewebes in diesen Organen einfach erklärt; ebenso die gelegentlich vorkommende Beteiligung dieser Drüsen bei Leukämie und Tuberkulose der Lymphdrüsen. Mir scheint aber mit dieser Annahme für die uns beschäftigende Krankheit noch nicht Alles erklärt.

Kehren wir zu den zuerst beschriebenen Fällen zurück, so müssen wir daran festhalten, dass es sich um eine chronisch verlaufende Erkrankung handelt, welche—soweit die bisherigen Beobachtungen lehren,—in den Thränendrüsen ihren Anfang nimmt und unter Umständen auf diese allein beschränkt bleibt. Die weitere Verbreitung des Prozesses erfolgt vorwiegend auf die Speicheldrüsen; die Beteiligung der Lymphdrüsen ist nur in den Fällen von Reymond und Adler beobachtet worden, falls wir diese Fälle überhaupt hierher rechnen. Nun gebe ich gern zu, dass die histologische Beschaffenheit der Intumescenzen und bis zu einem gewissen Grade auch der klinische Verlauf zu einem Vergleich mit den echten malignen Lymphomen nötigt; besonders auch der Umstand, dass in einzelnen Fällen nach Arsengebrauch ein zweifelloser Rückgang der Anschwellungen beobachtet worden ist. Es bestehen aber doch wesentliche Unterschiede zwischen den zwei Prozessen. Vor allem ist bisher in keinem der Fälle ein maligner Verlauf konstatiert worden. Wenn auch in dem Falle von Adler lange Zeit hindurch Arsen genommen wurde und somit der gutartige Verlauf auf das Medikament bezogen werden könnte, so wurde in meinem und dem Falle von Becker gar keine medikamentöse Behandlung eingeleitet, im Falle von Haltenhoff wurde nur Jodeisensyrup verordnet und im Falle von Fuchs musste die 2 mal eingeleitete Arsentherapie nach kurzer Zeit abgebrochen werden. Trotzdem (p. 629) trat im Falle von Haltenhoff vollständige Heilung ein, im Falle von Fuchs keine Pro-

gredienz des Prozesses, in meinem und dem von Becker nach der vollständigen Exstirpation kein Recidiv. Es ist mir nicht bekannt, dass maligne Lymphome auf Jodeisen so prompt reagieren; auch recidivieren nach meiner Erfahrung maligne Lymphome nach der Operation in kurzer Zeit.

Nach meiner Ueberzeugung handelt es sich hier um einen infektiösen oder parasitären Prozess im weitesten Sinne des Wortes. Man ist ja heute vielfach geneigt, auch in der Leukämie und Pseudoleukämie (maligne Lymphome) eine parasitäre Krankheit zu suchen; eine ähnliche Auffassung dürfte für unseren Krankheitsprozess ebenso berechtigt sein. Bei der Frage, ob wir uns den Krankheitserreger als einen hämatogenen oder einen von aussen in die Drüse eindringenden zu denken haben, möchte ich mich für die letztere Annahme aussprechen.¹ Dafür spricht die Lokalisierung der Krankheit auf die Drüsen der Gesichtsregion, sowie das Fehlen einer Miterkrankung des ganzen Organismus. Die Verbreitung des Prozesses auf scheinbar völlig getrennte Organe spricht nicht dagegen, wenn wir uns vorstellen, dass als Eingangspforten für den Krankheitserreger die Ausmündungskanäle der Thränen- und Speicheldrüsen in den Conjunctivalsack und die Mundhöhle dienen und dass der Conjunctivalsack durch Vermittlung des Thränennasenkanals und der Nasenrachen-schleimhaut mit der Mundschleimhaut ein Continuum bildet. Die Beobachtung, dass zuerst die Thränendrüsen und dann erst die tiefer gelegenen Speicheldrüsen erkranken, liesse sich dann so erklären, dass der Conjunctivalsack die eigentliche Eingangspforte abgibt, während die Mundhöhle erst sekundär von hier aus infiziert wird. Die Miterkrankung von Lymphdrüsen wäre dann auf dem Wege der Lymphbahnen nicht schwer zu erklären. In den Thränen- und Speicheldrüsen hätten wir uns den Prozess als einen ascendierenden nach Analogie der Entzündungsvorgänge in der Mamma, den Nieren, den Speicheldrüsen vorzustellen. Dem entsprechend müssten sich im ersten Anfang vielleicht auch krankhafte Veränderungen in der Conjunctival- und Mundschleimhaut finden, die durch denselben Krankheitserreger be-

¹ Vielleicht werden in künftigen Fällen die neuen Färbungsmethoden von Ehrlich, Biondi und Heidenhain sowohl über den Charakter der Geschwülste als auch über etwaige Veränderungen im Blut Aufschluss geben.

dingt sind. Wenn wir von diesem Gesichtspunkte aus die mitgeteilten Krankengeschichten durchsehen, so finden wir mehrere Angaben, dass die betreffenden Schleimhautabschnitte erkrankt waren, so in meinem (p. 630) Falle und in den Fällen von Becker und Adler die Conjunctiva, im Fall von Haltenhoff die Nasen- und Rachenschleimhaut.

Gegen die Auffassung eines ascendierenden Prozesses liesse sich einwenden, dass dann vorwiegend das eigentliche Drüsengewebe und nicht das interstitielle Gewebe beteiligt sein müsste. Wir wissen aber, dass das Drüsengewebe der Speicheldrüsen bei den verschiedenartigsten Prozessen, sowohl bei Neubildungen als auch bei entzündlichen Veränderungen sich in der Regel ganz passiv verhält oder erst sekundär in Mitleidenschaft gezogen wird. Sehr lehrreich ist für unsere Frage eine Arbeit von A. Hanau.¹ Dieser Forscher weist zunächst nach, dass die eitrige Parotitis auch bei akuten Infektionskrankheiten nicht hämatogenen Ursprungs ist, sondern als ascendierender Prozess aufzufassen ist, der sich von der Schleimhaut der Mundhöhle den Ausführungsgang entlang in die Drüse fortsetzt. Interessant ist es nun, dass die Entzündungserreger bald die Wand des Ausführungskanals durchdringen, die Bahn des Ganglumens gewissermassen auf halbem Wege verlassen und nun im lymphgefäßshaltigen, den Kanal umgebenden Bindegewebe in das interstitielle Gewebe der Drüse vordringen. Die Drüsenacini selbst sind am Prozess relativ wenig beteiligt.—

Doch genug der Hypothesen. Ich weiss wohl, dass den von mir ausgesprochenen Anschauungen sich leicht mit mannigfachen Argumenten begegnen lässt. Es wäre vielleicht einfacher und bequemer gewesen, sich auf die Mitteilung der Thatsachen zu beschränken. Wenn ich darüber hinausgegangen bin, so habe ich es nur in der Absicht gethan, die Gesichtspunkte anzudeuten, welche bei der Beobachtung künftiger Fälle ins Auge zu fassen sind. Hoffentlich gelingt es künftigen Beobachtern, die Rätsel zu lösen, die uns diese merkwürdige Krankheit stellt.—

¹ Ueber die Entstehung der eitrigen Entzündung der Speicheldrüsen. Beiträge zur path. Anat. von Ziegler und Nauwerck 1889. IV, 487.

ERKLÄRUNG DER ABBILDUNGEN AUF TAFEL IX

(Zu dem Aufsatz: Prof. Dr. J. Mikulicz, Ueber eine eigenartige symmetrische Erkrankung der Thränen- und Mundspeicheldrüsen.)

Fig. 1. Frisches Präparat der linken Submaxillar-Speicheldrüse. Natürliche Grösse.

Fig. 2. Dieselbe Drüse auf dem Querschnitt.

Fig. 3. Mikroskopisches Präparat von derselben Drüse. Hartnack Obj. 7.

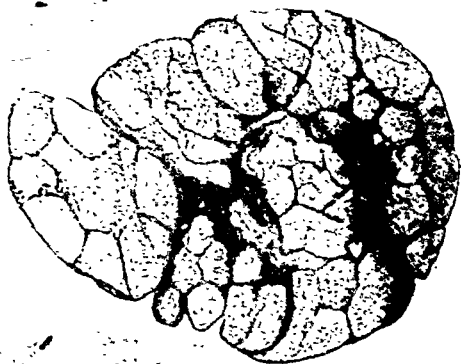
(Härtung in Flemming'scher Lösung, Färbung mit Saffranin.)

EXPLANATION OF THE ILLUSTRATIONS OF PLATE IX

Fig. 1. Fresh preparation of the left submaxillary Gland. Natural size.

Fig. 2. The same gland on transverse section.

Fig. 3. Microscopic preparation of the same gland. Hartnack Obj. 7.
(Fixed in Flemming's solution, stained with saffron.)





Concerning a Peculiar Symmetrical Disease of the Lacrymal and Salivary Glands

BY

PROF. DR. JOHANN MIKULICZ

Director of the Surgical Clinic in Breslau

With Plate IX and 5 Woodcuts

In the session of Jan. 23, 1888, I placed before the Society for Scientific Medicine at Königsberg¹ a case, which presented a peculiar symptom complex, until then unknown to me. Both lacrymal glands and all the salivary glands were changed in a symmetrical manner into tumors, which pushed themselves markedly forward from the normal position of these organs and thereby distorted the physiognomy of the patient in a remarkable way. The tumors had arisen gradually; they were at the time of examination of a hard consistency, painless, without trace of inflammatory signs. Moreover, elsewhere there were present no pathological changes in the bearer of these tumors.

The interpretation of this disease placed me in the greatest dilemma, for it occurred nowhere in the list of familiar and recorded diseases up to the present time. Also I found not a single observation similar to mine recorded in the literature. I had hopes that, perhaps accidentally, a second similar case would come into my hands and thereby I would be enlightened as to

¹ Berliner klin. Wochenschrift, 1888, 759.

the nature of the disease. However, this affection under discussion appears to be so rare, that I must give up this hope. Moreover, in the interval, many cases have been reported by other observers, which have been either entirely like mine or so similar that they can be included in a review of the disease process in question.

On this account I have resolved to report my case in detail today.

HISTORY OF PATIENT

A 42 year old, married farmer, Christof Kalweit of Marienwalde in East Prussia, had had pneumonia twenty years before; otherwise he had always been healthy. Seven months previously, in June, 1887, he noticed that both upper eyelids began to swell; he had no pain or other trouble, except that with the increased swelling, opening of the lids was rendered difficult. Later the palpebral fissure became so much narrowed that it was difficult for him to see. Soon afterward there appeared under both angles of the jaw, similar painless swellings, which, as they grew larger, interfered with eating and speaking. As to the time of development of other swellings, the patient could tell nothing, but in any case they first appeared at a later period. Only the disturbance in the use of his eyes alarmed the patient and brought him to a doctor, who prescribed for him an internal medicine. When this had no result, he sought help in the surgical clinic at Königsberg.

Condition on January 13, 1888. Strongly built, well nourished man of an otherwise healthy appearance. No demonstrable abnormality in the internal organs. Especially the liver, spleen and kidneys show no changes; urine is free from albumin. Pancreas not palpable. Prostate not enlarged. Nowhere does there appear any swelling of the lymph glands. In the blood there is no striking change, especially no leukocytosis. Tendon and superficial reflexes are normal; temperature and pulse normal.

The countenance appears strikingly altered because of the symmetrical swelling in the region of the upper eyelids, the parotid and the submaxillary glands. (See the accompanying illustration, Fig. A.) (See German text.)

The upper eyelids hang down so far, especially in their outer halves, that the palpebral fissure is reduced to a narrow, triangular space, with base formed by the inner two-thirds of the lower lid. In the outer third the two palpebral margins touch one another throughout. The patient is unable perceptibly to raise the upper lid himself, even with strong effort. Consequently the larger, upper and outer segment of the iris and pupil remain covered by the upper lid. Perhaps in consequence a convergent strabismus has developed, by which the pupils would appear in the relatively wide medial part of the palpebral fissure.

Moreover, the outer two thirds of the upper eyelids are arched forward and laterally as a hemisphere, so that here the middle fold of the lid appears nearly obliterated. On palpation there is found under the skin of the lid a small nodulated, firm tumor of an obliquely oval shape, which can be followed to the edge of the orbit. The tumor itself is but slightly movable, the mildly edematous skin of the lid, on the other hand, being easily displaceable over it. If the upper lid is drawn firmly upward with the finger, the outer half of the conjunctival fold appears so far pushed forward by the tumor described, that it reaches nearly to the edge of the cornea. (Compare the accompanying illustration, Fig. B.) (See German text.) The conjunctiva itself appears mildly reddened and somewhat thickened. The eyeballs are displaced somewhat inward and forward, but otherwise no pathologic changes are demonstrable. Vision is undisturbed.

The parotid region on both sides is occupied by a smooth, convex, solitary tumor, which corresponds in position exactly to the situation of the parotid gland; it extends forward to the middle of the cheek, continued in the niche between the ramus of the maxilla and the mastoid process and distinctly lifts up the lobule of the ear. It is firmly elastic in consistency. Its surface is apparently smooth, the overlying skin slightly movable.

Under each angle of the jaw projects a tumor about the size of a hen's egg, covered by normal, movable skin. It is somewhat displaceable and of a hard consistency; its surface can be recognized in some places to be flattened eminences. The two tumors almost meet in the midline.

If the patient opens his mouth, attention is drawn at once to tumors corresponding to the two sublingual glands. They present themselves as two oblong swellings, which, in form and size, resemble an almond placed on edge, occupy the floor of the oral cavity on both sides of the frenulum of the tongue. (See Fig. A, a-a.) They reach to the height of the crown of the teeth and lie between the tip of the retracted tongue and the row of teeth. The mucous membrane over the tumor is somewhat swollen.

The palatine glands show a marked enlargement. (See Fig. C.) (See German text.)

The palate on both sides is occupied by a sharply delineated swelling of almost the size of a chestnut, extending out over the edge of the soft palate. Both tumors extend to the alveolar border, but leave free in the midline a groove of normal appearance $\frac{1}{2}$ cm. wide, gradually increasing in width as it extends forward. Anteriorly they reach to the first premolar teeth. The surface of the swellings appears smooth, the overlying mucous membrane unchanged, the consistency firmly elastic.

Under the buccal mucous membrane there are found on each side of the excretory opening of Stenson's duct, movable nodules, about the size of a pea (accessory glands). In addition there lie further forward, in the vestibulum oris under the mucous membrane, many movable nodules up to pea size.

During the examination, a copious secretion of saliva takes place, but there is otherwise no sign of salivation existing. On the oral mucous membrane there is no striking change. Several teeth are missing, many are carious.

As only the swelling of the lacrymal glands was troublesome to the patient, in that it made the opening of the palpebral fissure difficult, a partial removal of these was undertaken at once (February 1, 1888). A horizontal incision was made about $1\frac{1}{2}$ cm. long in the direction of the palpebral fissure with a cleft of the conjunctiva over the most prominent part of the tumor. The gland was then freed by blunt dissection up to the ridge of the orbit and the denuded part removed with scissors. The

incision was sutured. On each side a mass of the tumor about $2\frac{1}{2}$ cm. long and 1 to $1\frac{1}{2}$ cm. in diameter was removed, by my reckoning about $\frac{2}{3}$ of the entire tumor. Primary healing followed. After only a few days the functional result was so evident that the patient could leave the clinic quite content.

The improvement in the condition did not last long. The tumors soon appeared again on the eyelids and narrowed the palpebral fissure almost to the same degree as before the operation. At the same time the tumors at the angles of the jaw visibly increased in size. For this reason the patient returned to the clinic the last of March. All the tumors seemed to have increased a little in circumference. The swelling of the lacrymal glands had reached very nearly to the original size. An attempt at treatment with pilocarpin injection was made in hopes of obtaining a decrease in the volume of the enlarged glands by the increased secretion. In spite of profuse salivation, the result was not satisfactory; therefore this was stopped after eighteen days treatment and at the urgent desire of the patient resort was again made to surgery. On the 19th of April, with an incision performed in the same manner as the first time, the entire lacrymal gland on the right side was extirpated. The last, deeply situated remaining portion was removed with a sharp curette. Good healing. On the 1st of May in the same way the other lacrymal gland was removed. At the same time the enlarged submaxillary glands on both sides were dissected out. They were lying somewhat less firmly in their beds than normal glands, and permitted enucleation without trouble and with but a slight amount of bleeding. There was good healing by primary intention. After ten days the patient was discharged.

Concerning the future lot of the patient, there are only accounts by letter. On July 12, two months after his discharge, he himself wrote me that he was very well satisfied with his condition. The swelling of the parotid glands seemed to have increased, but gave him no trouble. He was not hindered in the use of his eyes, although he had to work the whole day in the fields in the sun's heat. The swellings in the neck (submaxillary glands) had not reappeared. He felt in very good health.

On July 25 he was suddenly taken ill with signs of peritonitis (perityphilitis?), after he had worked all the day before. He died on the 9th day of the disease. The swellings in the parotid glands and in the mouth had so retrogressed within a few days during this sickness that they had almost disappeared before death.

Concerning the anatomic examination of the specimen removed, I can report the following: The submaxillary glands which had been removed in toto are most deserving of consideration. First of all it must be brought out that each of the glands, swollen to the size of a child's fist, corresponded exactly in relation to form and segmentation into lobes and lobules to the proportions of the normal gland. The full view and the transverse section, represented in Plate IX, Fig. 1 & 2, give a true representation. The tumor shows, in its gross microscopic details, the normal structure of the gland, only it is increased in mass. An essential difference is found, however, by the naked eye in the fresh transverse section in the color and finer structure of the glandular mass forming the individual lobules. In place of the finely granular, gray red structure of the normal gland substance, we see a more homogeneous, pale reddish yellow, amyloid mass of lesser transparency. Its consistency is decreased and very fatty. The number of blood vessels seems to be increased only in the septa, corresponding to the increase in the size of the organ; the substance of the glands seems remarkably poor in blood vessels.

The microscopic examination revealed that the main mass of the tumor was a pretty uniformly arranged tissue consisting of small round cells. (See Plate IX, Fig. 3) Here and there the cells lay compactly together; in other places a fine reticulum is to be seen between them. In single, large cells karyokinetic figures can be recognized. Imbedded in these small-celled main masses there appear, partly single and partly in groups, the apparently unchanged acini of the salivary gland; they are separated from one another in varying distances by the round cell tissue.

Similar relations present themselves in the microscopic examination of the lacrymal gland; only here the acini were found less frequently and, it seemed, were entirely lacking in the outer compressed part of the tumor.

As we try to explain the case just described, we strike on various difficulties. The disease process exhibits itself clinically as a slowly arising, huge enlargement of all the salivary and lacrymal glands, without inflammatory signs and without demonstrable general manifestations. The process remains sharply confined to the region of these glands and involves neither the neighboring structures nor other organs or tissues. The microscopic examination reveals that the true parenchyma of the glands plays an entirely passive rôle. The increase in size is entirely brought about by a massive, small-cell infiltration of the interstitial connective tissue.

It is clear that the microscopic findings alone cannot explain the process. Were a single gland involved in the way depicted, then we would not hesitate to postulate a true tumor. We know well enough that even in the salivary glands, the various tumors of the connective tissue series and, at times, even the round cell sarcoma occur, arising from the interstitial connective tissue. But the histologic finding here does not correspond to a typical round cell sarcoma; moreover the microscopic and still more the clinical findings speak against the picture of a genuine sarcoma. I refer to the preservation of the borders of the gland and particularly the large and small septa between the lobules of the glands. The histologic nature of the small cell infiltration corresponds primarily to the properties of a tumor of lymphoid tissue. Therefore one can think histologically of a lymphoma or lymphosarcoma.¹ Herewith we resign ourselves to an unsafe ground, to a field in which clinical observation and histologic investigation are not yet brought fully into accord and in which

¹ I have indeed regarded the process as belonging to a lymphosarcoma since the first microscopic examination and with this idea I have communicated the case to Herr Prof. Fuchs in Vienna.

the nomenclature is still inexact and ambiguous. We could think first of all of those forms of tumors which arise primarily from lymph glands or from preformed lymphoid tissue and then become designated as malignant lymphoma (pseudoleukemia). Heidenhain¹ has demonstrated lymphatic tissue in the interstitial connective tissue of the salivary glands, namely in the sublingual glands; therefore there is no objection to the assumption of a primary formation of lymphoma in the salivary gland. The entire lack of an involvement of the lymph glands and the spleen—as it accompanies the so-called pseudoleukemia of the skin, for example—speaks nevertheless against the character of a malignant lymphoma.

But also the theory of lymphosarcoma, arising occasionally away from the lymph glands, as in the testicles and in other organs, is not admissible in my opinion. According to my knowledge of cases of this kind, we always have to deal with malignant new growths, which sooner or later metastasize. The clinical course corresponds to that of typical sarcoma. The clinical course of our case during the 14 months of observation was not malignant in spite of the recurrence on the part of the lacrymal glands; in the last days of life of the patient, the undisturbed tumors rapidly decreased in size. If we consider further that the almost simultaneous appearance of the numerous seats of disease in the localized, completely separated places is directly contradictory to our experience with malignant tumor, we must decide to reject the acceptance of such an idea in our case.

The result of our consideration is therefore purely negative. Concerning the significance of the process, I can express only presumptions. But before I express the opinions which I have made in this direction, I should like to cite cases of other observers, insofar as they are to be used in reference to my case.

The case most similar to mine has been communicated briefly by Prof. Fuchs,² the lacrymal glands and parotids being diseased

¹ Studies of the Physiologic Institute of Breslau, 1868, Part 4, p. 116.

² Simultaneous Disease of the Lacrymal Glands and of the Parotid. *Beitrage zur Augenheilkunde*, v. III, 1891.

on both sides. In addition there is a case reported three years ago by Haltenhoff¹ with simultaneous swellings of the lacrymal glands, of the parotids and the submaxillary glands on both sides.

The case of Prof. Fuchs follows:

A 61 year old, well built man, a glazier by occupation, noticed, five months before, a swelling of the upper eyelids, and for four weeks before a tumor in the region of the parotid glands. Presented in the clinic of Prof. Fuchs in Vienna in March, 1890. Both upper eyelids were raised in their outer halves by a tumor which lay in the outer, upper part of the orbit. The anterior border of the swelling felt hard and uneven; the lids themselves were movable over it. If the lid were strongly elevated, the conjunctival fold in its outer half appeared bowed by a brown-red swelling. The bulbs were somewhat displaced anteriorly, otherwise normal. Vision was undisturbed.—Swelling of both parotid glands revealing itself as a flattened tumor of 4-5 cm. in diameter, which lay on the ascending ramus of the mandible and extended so far backward that the lobule of the ear appeared drawn away. In consistency hard, surface slightly uneven. The other salivary glands, as well as the lymph glands, were normal, likewise the testicles. Inner organs and blood normal. Syphilis not present.

The patient received Fowler's arsenical solution in daily increasing doses. He had reached only 14 drops when he suffered an acute eruption. After two months the lacrymal gland tumor on the right side was a little smaller, while that on the left remained unchanged. Also the swelling of the parotid regions, especially on the right side, had become considerably smaller. A further trial of the arsenic treatment had again to be broken off, because the patient got an eruption with chill and lost weight. In May, 1891, about fourteen months after the first presentation, Fuchs found nearly the same condition as the first time. All the swellings had again increased to nearly the original size. But they were still indolent, firm, nowhere adherent to the surrounding tissue, so that they seemed freely movable. The general condition was good.—At the first presentation of the patient Prof. Fuchs excised a small piece from that part of the lacrymal gland which protruded most prominently from beneath the upper conjunctival fold. On examination of this small portion, there appeared imbedded in the

¹Lymphatic Hyperplasia of the Lacrymal and Salivary Glands. *Annales d'oculistique*, 1889.

scarcely changed submucous tissue of the upper conjunctival fold, large and small nodules which showed the structure of lymphoma. Most of them were sharply walled off from the surrounding tissue; they consisted of densely crowded, mononuclear cells, with a nucleus round or slightly oval, densely granular and highly colored with the stain employed. In many nuclei the very faint cell protoplasm could be perceived arranged as a signet-ring; in most nuclei, however, a definite protoplasmic integument could not be seen. Between the cell elements there was no definite reticulum, but a very homogeneous intercellular substance. Single, thin-walled blood vessels were found in the interior of the nodules; nowhere was there a trace of disintegration or epithelioid or giant cells. Glandular elements were not to be found.

The history of the case of Haltenhoff's is briefly as follows:

A 12 year old girl had previously been treated in the eye clinic for a phlyctenular conjunctivitis. Four months before, swelling of the upper eyelids, in front of the ears and beneath the lower jaw developed by degrees, without known cause, without fever or complaint, occurring first in the right, then in the left eye, and finally in the other regions. She is a well developed child, of a somewhat pale appearance, otherwise healthy. There is a symmetrical forward bulging of the outer halves of the upper eyelids caused by a fixed tumor under the skin of the lid; no redness, no edema, no dilatation of blood vessels. The skin over the tumor is movable; the tumor itself smooth, hard, entirely painless, corresponding in position to that of the lacrymal gland. If the upper eyelid is raised, the conjunctival fold appears as if pushed forward by a red tumor. The conjunctiva of the bulb is otherwise normal. Both parotids are swollen in their entire extent to indolent, very hard tumors, which gives the child an appearance similar to that of mumps. The submaxillary glands are likewise converted into symmetrical tumors of a similar nature. In the sublingual glands no change is demonstrable. There is no swelling of the lymph glands. The internal organs are normal. The tonsils are somewhat enlarged, the mucous membrane of the pharynx slightly swollen. The teeth are intact, the gums and oral mucous membrane are of normal appearance. According to the statement of the mother, the child often coughs and breathes heavily; the mucus from the nose is frequently foetid. At present there exists an insignificant eczema of the nasal orifice. Salivary and tear secretion are not increased. Hemoglobin of the blood (Gower's method) is 85

per cent. Syrup of iodide of iron was ordered for the patient in addition to a strengthening diet and exercise in the fresh air. After fourteen days a decrease in the size of the swellings was noticed. More than a year later the girl had a healthy appearance. The submaxillary glands are no longer to be felt, but the parotids seem somewhat larger than normal. The lacrymal glands are to be plainly felt close to the ridge of the orbit.

I have given the two cases of Fuchs and Haltenhoff in some detail, because they are of significance for the characteristics of the disease process in question. Even though in the case of Haltenhoff no histologic finding is given, it agrees clinically so completely with the other two, that we can assume that we are dealing with the same process in all three cases. The case of Haltenhoff is especially of importance, because here, within a year's time, the very pronounced involution of the swellings had been substantiated.

Besides those quoted I find two other cases in the literature, which belong here in the greatest probability.¹ The case of Raymond² I know only through a report: A man of 57 years had had for two to three years a bilateral swelling of the upper eyelids, the parotid region and of the axillary glands. The tumor of the orbit was removed; the microscopic examination showed lymphoid tissue which revealed signs of amyloid degeneration in some places. The second case was presented as a sarcoma of the lacrymal glands in the year 1889 by Adler in the Society of Physicians in Vienna.³

I give the history of this sickness in abstract.

A man, 70 years old, had had no diseases except pneumonia and dysentery, and was not syphilitic. A year before he had noticed the appearance of swellings bilaterally in the region of the lacrymal glands, which gradually increased to their present size. Examination on April 3, 1889:—On the upper, outer edge of both orbits there are nearly

¹ By way of addition, Prof. Fuchs tells me that he has observed recently two cases analogous to the first, but of a milder nature. The swellings decreased after a month's treatment with arsenic. Leukemia was present in none of the cases.

² Arch. d'ophthalmologie, VI: 23.

³ Meeting of May 17, 1889. See Wiener klinische Wochenschrift, 1889, p. 422.

symmetrical tumors about $3\frac{1}{2}$ cm. long by 16 mm. broad; that on the right side is a protuberance about the size of a pea. The margin of the tumor projects outward and downward within the lid. The swellings are as hard as cartilage, have a nodular surface and are not painful; they are movable under the skin of the eyelid, but not so near the edge of the orbit and are fixed on the wall of the orbit. The palpebral fissure is narrowed in all its dimensions into a three cornered form with its point uppermost. There is an ectropion of the outer part of the left upper eyelid. On everting the upper lids one notices that the conjunctiva is degenerated in the region of the conjunctival fold and in part is occupied by a protuberance, the size of trachoma granules, in part by excrescences resembling cocks' combs. The conjunctiva of the bulb and tarsi is normal. Also for three months the patient has noticed various glandular swellings. At the present time the cervical, preauricular and submaxillary glands are swollen into hard nodules. For six weeks there has been hoarseness, for three weeks a "protrusion" of the hard and soft palate. In the pharyngeal space there is such a marked swelling that it is impossible to make an examination with the laryngoscope. Examination of a small piece removed from the conjunctiva showed a "small-cell sarcoma." It was assumed that a primary sarcoma of the lacrymal gland was present with a general sarcomatosis. For this reason all operative interference was abandoned and treatment with arsenic instituted. (Fowler's tincture, up to 10 drops daily.) After six weeks an apparent improvement occurred. The hoarseness disappeared, the swelling of the palates decreased, the tumors of the lacrymal glands visibly grew smaller so that they were only 2 cm. long by 11 mm. broad. Again the microscopic examination of an excised portion of the diseased conjunctiva confirmed the earlier histologic diagnosis; however, it was now, out of consideration of the result of the arsenic treatment, regarded as a lymphosarcoma or a malignant lymphoma. In the middle of September, 1892, almost four and one-half years after the onset of the illness, the patient is completely well according to a communication by letter from the physician-in-chief, Dr. Adler. He is still taking arsenic.

The two cases of Raymond and Adler differentiate themselves from the earlier ones essentially by the involvement of the lymph glands. The question therefore arises as to whether these cases in general belong here; a doubt in this direction appears all the more justified in that the disease of the salivary glands

was placed entirely in the background in the cases of Reymond and Adler. Moreover, Fuchs doubted that in the case of Reymond the parotids were involved; he believes that the lymph glands of the preauricular region had simulated a parotid tumor. In the case of Adler the salivary glands were not mentioned; nevertheless moderate swelling could escape observation among the enlarged preauricular and submaxillary glands. I might consider this possibility because in Adler's case a group of glands, which belong to the salivary type, certainly were swollen. I refer to the palatine glands. Those "protrusions" of the hard and soft palate I can only designate as such; they correspond also to the behavior of the palatine glands in my case.

The two cases have a striking similarity to the earlier ones in respect to the involvement of the lacrymal glands. The clinical course, especially the mildness of the process and the symmetrical devolvement correspond completely. The histologic findings do not oppose the acceptance of similar processes.

In our cases the involvement of the lacrymal glands is not the only constant finding; it is the one which first makes itself evident. We find in the history of the cases the definite statement that first the lacrymal glands swelled and later in a variable sequence the other swellings appeared. So it seems that the lacrymal glands serve as the first and principle point of attack of the excitant of the disease. For that reason, *a priori*, we could concede the possibility of an isolated disease of the lacrymal glands. And indeed we find in the literature many cases recorded of disease of the lacrymal glands alone, which, in my opinion, are to be included here. I disregard the commonly repeated statement of the text-books of "hypertrophy" of the lacrymal glands, as well as the numerous reports of case histories which allow only an uncertain interpretation. From the cases accessible to me I care to quote only three, first of all the accurately observed case of Arnold and Becker of the year 1872.¹

A 33 year old miller whose heredity was good, was well until 19 years of age. When 20 he was attacked by an inflammation of both eyes,

¹ Bilateral, Symmetrically Situated Lymphadenoma of the Orbits. Gräfe's Archiv., XVIII 2 Abt. 56.

which he attributed to the effect of dust from the mill. The inflammation of the eyes has persisted up to the present time in varying intensity and caused him repeatedly to seek medical aid. Since the 30th year of age there has been an exophthalmus. Feb. 1, 1871, he was admitted to the Heidelberg Eye Clinic. Both eyes protruded markedly from the orbits, their axes converging downward but their mobility to any side, nevertheless, not completely abolished. The upper lids of both eyes were markedly distended and for all practical purposes could not be raised at all. The conjunctiva in the whole extent was uniformly reddened, freely secreting; on the lower margin of the right cornea there was a development of blood vessels. Marked photophobia. Marked spontaneous pain was not present. As a cause of the exophthalmus there could be perceived a swelling in the upper, outer angle of each orbit, larger than a pigeon's egg, hard, non-pulsating, not painful on pressure, with a smooth surface. The swelling behind the right eye was considerably larger than the left. There was no connection with the eyeball.—It was assumed to be an hypertrophy of the lacrymal glands and extirpation of both tumors was performed through an incision parallel with the upper margin of the orbit. Early in June, 1872, both eyeballs had a normal position and range of motion. The tumor had not recurred. The conjunctiva of both eyes is loose, like velvet, and slightly injected, the conjunctiva of the eyeballs retiformly injected. No trace of trachoma granules. Increased secretion. Vision normal.—On Nov. 9, 1872, about one and three-fourths years after the operation, the tumors had not returned.

The examination undertaken by Prof. Arnold shows that the tumor is composed essentially of the lymphatic tissue. The compact accumulations of lymphoid elements which appear in a delicate reticulum and sharply delimited from the surrounding tissue, are exactly similar to lymph follicles. They lie in a more homogeneously arranged, diffuse lymphatic tissue. Here and there are stronger bands of connective tissue. Arnold did not hesitate to designate the tumor as a true lymphadenoma, that is, a new growth of lymphatic tissue. But in reference to the origin of this, he makes only suppositions. It is only with great difficulty that he can assume it to be a genuine heteroplasia, the development of a lymphatic tissue from the connective tissue of the orbit. It appears to him much more probably that at

the affected areas in the connective tissue of the orbit there is lymphatic tissue normally or in certain individuals, which has formed a point of origin for the tumor. But this is only an hypothesis, since proof, founded on fact, of such a kind of pre-formed tissue is lacking at this time.

Unfortunately I can find only very scant records concerning the other two cases. One was communicated in a few lines by Korn¹ under a reference to a case published by Horner of a symmetrical, acute inflammation of the lacrymal glands. The case concerned a female cigarette maker who suffered for four months with a swelling of the lacrymal glands. It was seen from the illustration accompanying the communication that it was a matter of a symmetrically lying tumor in the region of the lacrymal glands, which exactly, as in the other cases, presses the outer half of the conjunctival fold far downward.

The other case of Power,² I know only by reference. A boy of 16, otherwise well, suffered for half a year with a swelling of both lacrymal glands. After medication without success, the left lacrymal gland was extirpated. The microscopic examination disclosed an hypertrophy of the interstitial tissue, while no striking changes were found in the gland substance.

The incomplete data of the two last quoted cases does not permit them with certainty to be placed on a parallel with those of Becker, without any further information, and thereby to be added to our earlier cases. At any rate, they belong here in so far as they concern a chronic, symmetrically appearing tumor formation in the region of the lacrymal glands, benign in character. On the other hand, I hesitate to place the case of Becker directly into the category of earlier cases, in spite of the isolated affection of the lacrymal glands.

Accordingly, while we find observations recorded on an isolated disease of the lacrymal glands like the type described, we search in vain for similar references which relate to the salivary glands alone, to the exclusion of the lacrymal glands. Neither in the textbooks, nor in the pertinent monographs do we find this affec-

¹ Klinische Monatsblätter für Augenheilkunde, 1868, VII, 181.

² Transaction of the ophthalm., 1887, p. 109.

tion pointed out. The basic work of Billroth¹ on tumors of the salivary glands, the later, distinguished work of Kaufmann² on sarcoma of the parotid, and a recently appearing work of Nasse³ do not contain a single observation which could be applied here. It is also striking that, with the exception of my case, all observations introduced here originate from ophthalmologists.

I must not neglect to mention several other observations at this point, which pertain to the simultaneous affection of lacrymal and salivary glands and their respective lymph glands, but which, except for this similarity, have little in common with our case. First a case of acute inflammation of both lacrymal glands following an epidemic parotitis in an 11 year old girl, reported by Gordon Norrie⁴ which the author probably correctly took to be a true mumps of the lacrymal gland. Then Galexowski⁵ reported a case of acute inflammation of the lacrymal glands which he observed in a woman 40 years of age; the affection was accompanied by a swelling of the preauricular and submaxillary lymph glands. Furthermore, Scheffels⁶ reported a case of bilateral, nonsuppurative dacryadenitis with no elevation of temperature. The malady was not painful. At the same time the submaxillary, salivary and lymph glands were swollen to the size of a child's fist; moreover, swellings of lymph glands were found elsewhere and also an enlargement of the spleen. Parotid and preauricular glands were unchanged. With the use of potassium iodide, the swellings receded within 13 days. Horner⁷ also reported a case of acute, indolent, fever-free enlargement of both lacrymal glands. Here also the swelling receded within three weeks with the use of potassium iodide. Accompanying symptoms on the part of salivary and lymph glands were lacking.

Of chronic processes which have a certain similarity to the

¹ Observations on Tumors of the Salivary Glands, Virchow's Archiv. XVII, 357.

² Parotid-Sarcoma. Arch. f. klin. Chir., XXVI, 672.

³ The tumors of the Salivary Glands and Related Tumors of the Head. Arch. f. klin. Chir., XXXIV, 233.

⁴ Centralblatt, f. Augenheilk., 1890, 223.

⁵ Recueil d'ophthalmologie, 1886, 415.

⁶ Centralbl. f. Augenheilk., 1890, 136.

⁷ Klinische Monatsblätter, 1866, IV, 257.

affection with which we are concerned, as far as I know, only the leukemic enlargement and tuberculosis of the lacrymal glands accompanying the same affection of the lymph glands present themselves.

Gallasch¹ described a case of leukemia of this type. It occurred in a 4½ year old girl, who suffered from typical leukemia and also succumbed to this malady. Besides the enlargement of spleen, liver and the lymph glands in various regions, the lacrymal glands, the parotids and the sublingual glands were also swollen. Gallasch found the lacrymal glands taken up by a leukemic tumor in the same manner as the other diseased glandular organs.

Cases of this type appear to be very rare, at least I find no further observation in the literature. Indeed, a tuberculous infiltration of the lacrymal gland may be just as rare. I have observed a characteristic case of this kind in Königsberg. The affection of both lacrymal glands followed the development of numerous tuberculous lymphomata of the parotid and submaxillary region. I give the case in detail because of its rareness.

Edward Stein, 20 years of age, a miller from Rogehnen in East Prussia. The father suffers from a pulmonary ailment, the mother and three brothers are healthy. The young man, previously always healthy, noticed the appearance of a lump about the size of a hazelnut beneath the chin one year ago. Soon new nodes appeared in the vicinity; they grew relatively rapidly for a few weeks but then increased imperceptibly in size. Thus the swelling of the face and neck now present developed in the course of eight to ten months. Four weeks ago the patient first noticed the tumor in the left upper eyelid. He has never been troubled by it.—For some time he has suffered from cough.—Findings on May 2, 1889. Powerfully built, well nourished man of an otherwise healthy appearance. Both submaxillary regions occupied by conglomerate lumps of bean to hazelnut sized glands. (See accompanying Figure D.) The single glands are smooth, of firm consistence, displaceable individually as well as in toto within reasonable limits upon the underlying structures. The skin over them is unchanged and movable. The left sided group of glands is greater in circumference

¹ Bilateral Leukemic Infiltration of the Lacrymal Glands. *Jahrb. für Kinderheilkunde*, 1874, VII, 1, p. 82.

than that on the right and joins directly with a second group of partly conglomerate, partly isolated glands in the masseteric and parotid region. These bean- to cherry-sized glands extend to the zygomatic process and lie for the most part on the parotidomasseteric fascia. The preauricular glands are swollen to the size of beans. A smaller group of glands is found in the right parotid region. An additional continuous train of glands of the same size runs along the anterior and posterior borders of the left sternocleidomastoideus down to the clavicle. All the individual glands here have the same properties as those first described. In addition, the submental, cervical, axillary, cubital and inguinal glands are moderately swollen and hardened.

The outer two-thirds of the left upper eyelid is markedly arched anteriorly and broadened. The affected section of the edge of the lid appears deeper than its fellow and the palpebral fissure narrowed. The examining finger finds a cylindrical tumor about 2 cm. long, smooth of surface and of elastic consistence beneath the otherwise unchanged skin of the lid. The tumor can be followed to the orbital edge in all places and appears to be firmly attached to the superior orbital wall. No demonstrable changes in bulb or conjunctiva. By palpation at the analogous spot on the right upper orbital border a flat, firm tumor attached to the orbital wall may be demonstrated, the anterior edge of which just reaches the border of the orbit.—Splenic dullness somewhat enlarged, the spleen, however, is not palpable. No demonstrable changes in the rest of the internal organs. No increase in leucocytes.—

An attempt at arsenic therapy (internal) was first made, on the assumption that it was malignant lymphoma. Since the patient could not tolerate the gradual increase of massive doses at all, the tumor on the left eye was removed in accordance with his wish. Horizontal incision 1 cm. long, prolonging the palpebral fissure, splitting of conjunctiva over the tumor, extirpation of the whole lacrymal gland with forceps and scissors. Suture up to the outer corner of the wound, through which a narrow strip of iodoform gauze was placed into the cavity of the wound. Healing with slight amount of suppuration.—

The main mass of the lacrymal gland, which was enlarged probably ten times, consists of granulation tissue; in this are numerous typical tubercles with Langhans' giant-cells.

Perhaps a case reported by Frost¹ is also to be regarded as tuberculosis. Here the swelling had come on during the course

¹Transaction of the ophthalm., 1887, 109.

of nine months. The microscopic investigation of the extirpated gland showed that the tumor consisted essentially of a small-celled tissue resembling granulations that had caused a large part of the proper glandular substance to atrophy. Regressive changes were found in some places, ceseation in two.

The last described cases of acute and chronic diseases of the lacrymal glands are of importance to us because they show, (1) that a bilateral involvement of the lacrymal glands occurs in various affections, that it is not alone characteristic of the disease in which we are interested, and (2) that a certain alternating relationship exists between lacrymal and salivary glands as well as between lacrymal and neighboring lymph glands. One can only surmise as to what this alternating relationship is based on. Perhaps it is due to the fact that there are normally small lymphatic elements in the lacrymal gland as well as in the salivary gland, that is in the connective tissue surrounding them and running through them. Thus the formation of pathologic lymphoid tissue in these organs is simply explained, likewise the incidental involvement of these glands in leukemia and tuberculosis of the lymph glands. However, it appears to me that this assumption does not explain everything about the disease with which we are concerned.

If we return to the cases first described, then we must cling to the fact that we are concerned with a chronically running disease, which—so far as the observations up to the present teach us—begins in the lacrymal glands and under certain circumstances remains limited to these alone. The further extension of the process takes place in the salivary glands; the participation of the lymph nodes has been observed only in the cases of Reymond and Adler, if we include these cases here. Now I am willing to admit that the histologic characteristic of the intumescences and also, to a certain extent, the clinical course necessitates a comparison with the true malignant lymphoma; especially also the fact that in some cases after the use of arsenic regression of the swelling without a doubt has been observed. But nevertheless there are essential differences between the two processes. Above all, up to the present, in none of the cases

has a malignant course been substantiated. Even if arsenic was taken for a long time in Adler's case and the benign course there could be attributed to the medication, in my case and that of Becker no medicinal therapy was introduced at all, in Haltenhoff's case only syrup of iodide of iron was prescribed and in Fuch's case the arsenic therapy introduced on two occasions had to be stopped after a short time. Nevertheless, in Haltenhoff's case complete cure occurred, in Fuch's there was no progression of the process, in that of Becker and in my case there was no recurrence after complete extirpation. I do not believe that malignant lymphoma reacts so promptly to iodide of iron and in my experience malignant lymphoma recurs a short time after operation.

According to my convictions, we are concerned here with an infectious or parasitic process in the broadest sense of the word. Indeed at the present time there is a great tendency to look for a parasitic infection in leukemia and pseudoleukemia (malignant lymphoma); a similar idea would be justified in our disease. In regard to the question as to whether the causative agent is to be looked upon as hematogenous or as penetrating the gland from the outside, I am in favor of the latter assumption.¹ The localization of the disease to the glands of the region of the face, as well as the lack of a general disease of the whole organism, speaks in favor of this. The extension of the process to apparently completely separated organs is not to the contrary, if we keep in mind that orifices of the ducts of the lacrymal glands and salivary glands in the conjunctival sac and oral cavity serve as portals of entry for the causative agent and that the conjunctival sac is continuous with the mucous membrane of the mouth by way of the naso-lacrymal duct and the nasopharyngeal mucous membrane. The observation that the lacrymal glands are first affected and then the deeper lying salivary glands, is thus easily explained in that the conjunctival sac is the primary portal of

¹ Perhaps the new staining methods of Ehrlich, Biondi and Heidenhain in favorable cases will give some explanation as to the character of tumors as well as some of the changes in the blood.

entry, while the oral cavity is only secondarily infected from here. The sympathetic affection of lymph glands by way of the lymphatics then would not be difficult to explain. We should have to conceive of the process in the lacrymal and salivary glands as an ascending one analogous to the inflammatory processes in breast, kidneys and salivary glands. Perhaps in the beginning, corresponding pathologic changes in the conjunctival and oral mucous membrane, caused by the same agents ought to be found. If we regard the case histories reported from this point of view, we find many statements that the portions of mucous membrane concerned were diseased, as in my case and the cases of Becker and Adler the conjunctiva, in Haltenhoff's case the mucous membrane of the nose and throat.

The objection to the proposition of an ascending infection can be raised that the proper glandular tissue and not the interstitial tissue ought to be affected. But we know that the glandular tissue of the salivary glands, as a rule, remains entirely inactive and is only involved secondarily in various processes, in neoplastic, as well as in inflammatory changes. A work of A. Hanau¹ is very instructive on this question. This investigator demonstrates that the suppurative parotitis of acute infectious diseases is to be regarded not as of hematogenous origin but as an ascending process, which proceeds from the mucous membrane of the mouth along the duct into the gland. Now it is interesting that the inflammatory agents soon penetrate the wall of the excretory canal, leave the track of the lumen of the passage, so to speak, at the half-way point, and penetrate the interstitial connective tissue of the gland via the lymphatic-containing connective tissue surrounding the duct. The glandular acini themselves play little part in the process.—

Enough of hypotheses. I well know that the views which I have expressed easily allow of much argumentation. Perhaps

¹On the Origin of Suppurative Inflammation of the Salivary Glands. *Beitrag zur Path. Anat. von Ziegler and Nauwerck*, 1889, IV, 487.

it would be simpler and easier to limit the report to facts. If I have gone beyond them I have done so only with the purpose of making clear the points which are to be noted in the observation of future cases. I hope that future observers will succeed in solving the riddle which this remarkable disease presents to us.—

(THE END)

MIKULICZ OPERATION—COLECTOMY

To Mikulicz belongs the credit of popularizing resection of a carcinoma of the intestine by the two stage method. Before him the single stage resection with primary suture gave a terrible mortality. If Mikulicz were not so frank and honest in giving the honor of the invention to another (Block), we could believe that the idea had been spontaneously born in his own genial brain. But to this great pupil of the master Billroth, the medical profession is indebted, as far as treatment of intestinal cancer goes, because of the careful study and report of this type of case. Mikulicz gave detailed figures of final results of 106 cases; most striking is his ability to reduce a mortality of 42.9 per cent following resection with primary suture to 12.5 per cent with the two stage method. A form of two stage resection had been used previous to this report in cases necessitating rapid completion of an operation because of the poor condition of the patient. Mikulicz advised the operation as one of choice in being safer from every angle; he advanced beyond Block in removing the mesentery and regional lymph nodes with the involved portion of intestine. Truly it is a small homage to pay to this great mind to remember his name at least, in speaking of an operative procedure which has been of such value.

The article here given in the original form with English translation by Dr. W. de Rouville and myself is the same one mentioned in *An Exhibit of Important Books, Papers and Memorabilia as Illustrating the Evolution of the Knowledge of Cancer* by Haagensen, C. D., Amer. J. Cancer, 18: 98, 1933.



Chirurgische Erfahrungen über das Darmcarcinom¹

VON

J. VON MIKULICZ

in Breslau

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MEINE HERREN! Die chirurgische Behandlung des Darmcarcinoms war schon wiederholt in unserer Gesellschaft Gegenstand eingehender Besprechung. Ich brauche nur an den lehrreichen Vortrag des Herrn Koenig aus dem Jahre 1890, an die Mittheilungen des Herrn von Bramann aus dem Jahre 1898 und an die eingehende Darstellung des Herrn Koerte zu erinnern, der vor 2 Jahren über 54 einschlägige Fälle berichten konnte. In demselben Jahre hat De Bovis in der *Revue de Chirurgie* eine kritische Zusammenstellung von annähernd 450 chirurgisch behandelten Fällen von Darmcarcinomen gegeben, unter einer wohl erschöpfenden Berücksichtigung der in der Literatur niedergelegten Erfahrungen. Es könnte demnach fast überflüssig erscheinen, den Gegenstand wieder zur Sprache zu bringen. Und doch wird jeder Chirurg sowohl nach seinen eigenen Erfahrungen als auch nach der Durchsicht der Literatur der Ueberzeugung sein müssen, dass wir noch weit entfernt von einem Abschluss in der ganzen Frage stehen. Wenn wir auch heute schon sagen können, dass das Darmcarcinom eines der dankbarsten Gebiete der Abdominal-Chirurgie

¹ Vortrag, gehalten auf dem 31. Congress der Deutschen Gesellschaft für Chirurgie.

abgiebt, so lassen unsere Resultate doch noch manches zu wünschen übrig. Sie müssen durch eine Vervollkommnung der Technik besser werden; sie müssen auch besser werden durch ein eingehenderes Studium der klinischen Erscheinungsformen des Darmcarcinoms; denn dadurch werden wir (p. 29) in die Lage versetzt, das Leiden früher zu erkennen und in einem früheren Stadium einer chirurgischen Behandlung zu unterziehen. Vielleicht werden meine bescheidenen Erfahrungen einen kleinen Beitrag dazu liefern.

Im Laufe der letzten 11 Jahre kamen in der Breslauer Klinik 106 Fälle von bösartigen Darmgeschwülsten—mit Ausschluss des Mastdarms—zur Beobachtung. 5 mal handelte es sich um Sarkom, und zwar 3 mal am Dünndarm, 2 mal am Dickdarm. Einmal lag ein Endotheliom des Colon transversum vor. 100 mal handelte es sich um Carcinom, welches 5 mal am Dünndarm, 95 mal am Dickdarm sass.

Da das Darmsarkom wohl in den meisten Fällen unter demselben klinischen Bilde wie das Darmcarcinom verläuft, so darf ich vom practischen Standpunkte aus bei der folgenden Besprechung beide Geschwulstformen zusammenfassen.¹

Dem Geschlechte nach waren es 80 Männer und 26 Frauen. Ein so starkes Ueberwiegen des männlichen Geschlechtes (3:1) kommt meines Wissens in den anderen Statistiken nicht zum Ausdruck. Bei De Bovis ist das Verhältniss der Männer zu den Frauen 54:46.

In Bezug auf das Alter sind gerade beim Carcinom bei mir alle Altersstufen vom 2. bis. 8. Lebensdecennium vertreten. Die jüngste Patientin war 16 Jahre alt. Ueber die Vertheilung der Fälle nach Alter und Geschlecht giebt folgende Tabelle Aufschluss:

¹ Die unter Umständen augenfälligen Unterschiede im klinischen Verlaufe des Darmcarcinoms und Sarcoms, namentlich das raschere Wachsthum und das mitunter vollständige Fehlen von Stenosenerscheinungen beim Darmsarcom sind für den einzelnen Fall zur Differentialdiagnose nur mit Vorsicht zu verwerthen, da wir auch bei den verschiedenen Formen des Darmcarcinoms die grössten Unterschiede nach beiden Richtungen beobachten. Eine eingehendere Besprechung findet sich in den einschlägigen Kapiteln des dritten Bandes des Handbuches der praktischen Chirurgie von v. Bergmann, v. Bruns und v. Mikulicz.

Alter	Männer	Frauen	Zusammen
Unter 20	—	1	1
20-29	3	1	4
30-39	10	5	15
40-49	19	3	22
50-59	23	10	33
60-69	21	6	27
70-79	3	—	3
über 80	1	—	1

(p. 30) Nach der Höhe des betroffenen Darmabschnittes waren die Geschwülste folgendermassen vertheilt:

a) Dünndarm 8 Fälle (5 mal Carcinom, 3 mal Sarkom).

b) Coecum 20 Fälle (19 mal Carcinom, 1 mal Sarkom).

c) Colon (mit Ausschluss des Coecums und der Flex. sigmoidea) 40 Fälle und zwar:

α) Colon ascendens: 6 Fälle.

β) Flexura hepatica: 7 Fälle.

γ) Colon transversum: 8 Fälle.

(7 mal Carcinom, 1 mal Endotheliom)

δ) Flexura lienalis: 12 Fälle.

e) Colon descendens: 4 Fälle.

ς) Colon ohne genaue Localisation 3 Fälle.

d) Flexura sigmoidea 31 Fälle.

e) Ausgangspunkt unbekannt¹ 7 Fälle (1 mal Sarkom, 6 mal Carcinom).

Die angeführten Zahlen stimmen mit den anderen z. Th. viel grösseren Statistiken gut überein, indem sie ergeben, dass als Praedilectionsställe des Darmcarcinoms in erster Linie die Flexura sigmoidea, in zweiter Linie das Coecum anzusehen sind.

So gesetzmässig das Darmcarcinom sich auf die verschiedenen Abschnitte des Darms vertheilt, so regellos scheint sich der klinische Verlauf in den einzelnen Fällen zu gestalten, wenn wir zunächst davon absehen, dass die Höhe des erkrankten Darmabschnittes von einem gewissen Einfluss auf die Entwicklung der

¹ Die Fälle mit unbestimmter Localisation beziehen sich auf nicht operirte Patienten, bei denen die Diagnose durch die klinischen Erscheinungen, einige Male, wie in einem Falle von Darmsarkom, auf Grund von exstirpirten Lymphdrüsen gestellt werden konnte.

klinischen Erscheinungen ist. Es ist ja bekannt, dass ein Tumor, wenn er einmal ausgesprochene Functionsstörungen im Darne hervorruft, nicht gleichartig verläuft, je nachdem er im Dünndarm, im Bereiche des Coecums oder in den tieferen Dickdarmabschnitten sitzt. Man kann im allgemeinen sagen, dass, je höher das Darmcarcinom (p. 31) sitzt, die Erscheinungen um so praegnanter und die Störungen um so stürmischer verlaufen. Wenn wir aber von der Localisation absehen, so kann ein Darmtumor an ein und derselben Stelle das eine Mal lange Zeit ganz latent verlaufen, das andere Mal unklare Intestinalerscheinungen, das dritte Mal chronische Stenoseerscheinungen, das vierte Mal plötzlich acuten Ileus verursachen. Wir werden uns über die Verschiedenheit des Verlaufes nicht wundern, wenn wir überlegen, dass ein Darmtumor an und für sich noch keinerlei Symptome zu setzen braucht, da er sich in einem Organe festsetzt, das, wie wir wissen, keine sensiblen Nerven besitzt. Die Beeinträchtigung der Peristaltik infolge der Infiltration der Darmwand an einer beschränkten Stelle wird für den Gang des Verdauungsgeschäftes auch ohne Belang sein, da die darüberliegenden Darmparthien kräftig genug sind, für das peristaltisch unthätige Darmstück vicariirend einzutreten. Erst Complicationen werden das Darmcarcinom klinisch bemerkbar machen. Diese sind Stenose, Ulceration und Blutung. Die letzten zwei Complicationen werden sich in der Regel nur bei tief sitzenden Carcinomen, im Bereiche der Flexur event. des Colon descendens durch Beimengung von Blut und Eiter zum Stuhle sicher kenntlich machen; die Blutung auch bei höherem Sitze, wenn sie profus wird, doch ist das bekanntlich gerade beim Darmcarcinom ein seltenes Ereigniss. Als die constanteste Complication, die fast in jedem Falle früher oder später eintritt, dürfen wir die Stenose ansehen, doch ist sie, wie wir wissen, leider kein Frühsymptom. Die meisten Carcinome setzen wohl sehr bald eine Stenose im anatomischen Sinne, aber diese braucht noch lange nicht zur Stenose im klinischen Sinne, das ist zur Behinderung der Darmpassage an der betreffenden Stelle, zu führen. Der über der Stenose liegende Darmabschnitt compensirt infolge einer stetig zunehmenden Arbeitshypertrophie lange Zeit die anatomische Stenose und häufig in so vollkommener

Weise, dass keine functionellen Störungen bemerkbar zu sein brauchen. Wie weit diese Compensation gehen kann, beweisen am besten jene Fälle, in welchen ein bis dahin anscheinend gesunder Mensch an acutem Ileus erkrankt, als dessen Ursache man ein schon hochgradig stenosirendes Darmcarcinom findet. Die klinische Darmstenose tritt eben erst ein, wenn infolge der dauernden Stauung oberhalb des Darmcarcinoms schwerere Erscheinungen von Darmkatarrh sich (p. 32) einstellen, wenn infolge der ungenügenden Passage durch die stenosirte Stelle der Darm zu forcirter, krampfartiger Peristaltik gezwungen wird (Darmsteifung), oder wenn durch ein zufälliges Ereigniss (kleine Fremdkörper, entzündliche Schwellung) die verengte Stelle plötzlich ganz undurchgängig wird. Ich kann es unterlassen, an dieser Stelle auf die bekannten Erscheinungen der chronischen Darmstenose sowie des acuten Darmverschlusses näher einzugehen. Ich möchte nur betonen, dass das Darmcarcinom häufig auch bei längerem Bestande symptomlos oder mit nicht charakteristischen Erscheinungen verlaufen kann, dass man daher auch bei scheinbar unbedeutenden Störungen der Darmfunction bei der Diagnose ein Carcinom mit in die Combination ziehen soll, besonders wenn die Erscheinungen bei einem älteren Menschen auftreten, der bis dahin sich einer tadellosen Verdauung erfreut hat. Nicht selten wird man dann durch eine genaue Untersuchung des Abdomens, durch Aufblähung des Darmes und andere Untersuchungsmethoden einen palpablen Tumor oder sonst wie Indicien auf einen Darmtumor finden, und zwar lange, bevor noch schwerere functionelle Störungen aufgetreten sind.

Dass die histologische Form des Carcinoms auch dafür bestimmend wirkt, ob eine hochgradige Stenose früh oder spät eintritt, darf ich ebenfalls als bekannt voraussetzen. Auffallend sind in dieser Richtung die Gegensätze, die man zwischen den klinischen Erscheinungen bei grossen umfänglichen und bei kleinen, durch die Bauchdecken gar nicht palpibaren Tumoren findet. Ein grosser, relativ weicher, aber nach dem Darmlumen zu weit ulcerirter Tumor kann ohne schwere Behinderung der Darmpassage verlaufen, während ein kleines, auf wenige Centimeter beschränktes scirrhoeses Carcinom in Folge der starken Schrump-

fung schon frühzeitig schwere Stenoseerscheinungen bedingen kann. Namentlich im Bereiche der Flexura sigmoidea sind die Carcinome der letzten Art nicht selten.

Es ist vielleicht nicht unzweckmässig, die Darmcarcinome nach ihrem klinischen Verlaufe oder nach den Stadien, die der einzelne Fall durchgeht, nach verschiedenen Typen zu gruppieren, wie es z. B. De Bovis thut, welcher drei Typen unterscheidet:

1. Types de latence absolue ou relative.
2. Types gastrointestinales.
3. Types d'occlusion grave.

(p. 33) Diese Einleitung hat gewiss ihre Berechtigung, da die meisten Fälle wenigstens zwei, vielleicht alle drei Stadien nach einander durchmachen.

Ich möchte von einem anderen, mehr praktischen Standpunkte im Verlaufe des Darmcarcinoms folgende drei Perioden unterscheiden:

- A) Latenzperiode.
- B) Periode der Initialsymptome.
- C) Periode der klinisch nachweisbaren Symptome.

A) In Bezug auf die Latenzperiode können wir selbstverständlich nur Vermuthungen aussprechen. Die später angeführten Beobachtungen, nach welchen ein zufälliger Weise im Abdomen palpirter Tumor, das erste Symptom eines Darmcarcinoms abgiebt, Fälle, in welchen ohne Prodromalerscheinungen plötzlich acuter Ileus infolge eines Darmtumors auftritt, sprechen dafür, dass das Darmcarcinom lange, jedenfalls viel länger als man allgemein annimmt, latent verlaufen kann. Auch die Beobachtungen, nach welchen ein Kranker mit Darmcarcinom nach der Colostomie noch mehrere Jahre (ein Fall meiner Beobachtung $4\frac{1}{2}$ Jahre) bei relativem Wohlbefinden weiterleben kann, spricht in demselben Sinne. Diese Beobachtungen sprechen auch dafür, dass das Darmcarcinom entgegen der Anschauung der meisten inneren Kliniker ein relativ gutartiges Carcinom ist, gutartig auch deshalb, weil Drüsenmetastasen und Metastasen in anderen Organen in vielen Fällen erst spät auftreten. Wir müssen dies hervorheben, weil es in hohem Grade für die Berechtigung der operativen Therapie beim Darmcarcinom spricht, was heute auch

noch von Seiten der inneren Kliniker zu wenig anerkannt wird. Wenn ich auf Grund einer Schätzung Zahlen angeben soll, so möchte ich die Latenzzeit beim Darmcarcinom auf $\frac{1}{2}$ —3 Jahre anschlagen.

B) Was die Initialsymptome betrifft, so können sie sich, wie schon aus den vorangehenden Bemerkungen hervorgeht, ausserordentlich mannigfaltig gestalten. Ich verstehe darunter diejenigen Symptome, welche den Patienten zum ersten Male auf sein Leiden aufmerksam machen, gleichgiltig ob er alsbald ärztlichen Rath aufsucht oder nicht. Nach meinen Beobachtungen möchte ich zwei Gruppen sondern.

a) Fälle ohne charakteristische Störungen der Darmpassage; (p. 34) dahin gehören 58 der 106 von mir beobachteten Fälle, also mehr als die Hälfte und zwar wurden angegeben;

1. 43 mal unklare gastrointestinale Erscheinungen, meist als Unregelmässigkeit in der Stuhlentleerung beobachtet, indem entweder Obstipation oder Neigung zur Diarrhoe bestand oder beide Zustände abwechselten.

2. 9 mal wurde ein Tumor im Abdomen zufälliger Weise bemerkt, ohne irgend welche Störungen von Seiten des Darmes; ausserdem wurde noch 12 mal ein Tumor neben den früher angeführten unklaren gastrointestinalen Störungen bemerkt.

3. 6 mal waren es locale peritonitische Erscheinungen, die offenbar von dem ulcerirten zur Perforation führenden Tumor ausgingen; 5 mal handelte es sich dabei um einen Coecaltumor, der später unter dem Bilde einer Perityphlitis mit Abscedirung verlief, 1 mal trat ohne vorhergehende Prodromalerscheinungen Perforation in die Blase ein: Cystitis mit Pneumaturie war das erste allarmirende Symptom.

b) Fälle in welchen die Erscheinungen sich in deutlichen Störungen der Darmpassage äusserten, 48 mal. Darunter 39 mit Zeichen der chronischen Darmstenose, 5 mit acutem Ileus ohne Prodromalerscheinungen; 4 Fälle können als chronischer Ileus, d. i. als Grenzfälle zwischen chronischer Darmstenose und acutem Ileus angesehen werden.

C) Die Periode der klinisch nachweisbaren Symptome als ein besonderes Stadium der Erkrankung anzusehen, ist selbstver-

ständig etwas ganz willkürliches, denn das Eintreten dieses Stadiums hängt ja vor allem davon ab, wann der Kranke Hilfe in einer klinischen Anstalt sucht. Vielfach, z. B. in allen Fällen von Ileus wird dieses Stadium mit dem Initialstadium zusammenfallen. Immerhin gestattet uns aber eine derartige Gruppierung zu beurtheilen, wie weit wir die Diagnose zu einer Zeit sichern können, in welcher der Patient sich schon für so schwer krank hält, dass er ernstlich Hilfe sucht, namentlich von Seiten eines Chirurgen. Von den 106 Fällen, die bei uns Hilfe suchten, zeigten 84 (80 pCt.) schon ausgesprochen functionelle Störungen von Seiten des Darms und zwar waren 45 mal Zeichen einer ausgesprochenen meist schweren chronischen Darmstenose vorhanden, 28 mal acuter Ileus (dazu kommen noch 2 Fälle, die wegen Ileus ausserhalb der Klinik (p. 35) colostomirt worden waren), 11 mal handelte es sich um chronischen Ileus.

Nur 22 mal (20 pCt.) fehlten typische functionelle Darmstörungen. Der Darmtumor machte in diesen Fällen folgende Erscheinungen:

1. 7 mal beschränkte sich dies Symptom lediglich auf einen palpibaren Tumor im Abdomen.

2. 8 mal waren Zeichen der Perforation vorhanden, und zwar je 1 mal Perforation in die freie Bauchhöhle mit Peritonitis, Perforation in die Blase, Perforation in den Magen, 5 mal war ein perityphlitischer Abscess vorhanden.

3. In 7 Fällen lagen auch zur Zeit der klinischen Beobachtung nur unklare Gastrointestinalerscheinungen vor.

Wir sehen also, dass zur Zeit der klinischen Beobachtung mit Ausnahme von 7 Fällen immer schwere Erscheinungen vorlagen, welche die Diagnose eines Darmtumors oder wenigstens eines stenosirenden oder ulcerirenden Darmprocesses anzeigten. Für den Chirurgen war also in diesen Fällen die Diagnose genügend sicher gestellt, um die Frage, ob ein operativer Eingriff am Platze sei oder nicht, zu beantworten. Es würde mich zu weit führen, hier auf die Schwierigkeiten in der Differentialdiagnose zwischen dem Darmcarcinom und anderen ulcerirenden und stenosirenden Processen des Darmes näher einzugehen. Häufig genug wird sich der Chirurg mit der allgemeinen Diagnose „Darmtumor“ oder

„Darmstenose“ begnügen müssen, und wenn keine Contraindicationen vorliegen, wird schon die Möglichkeit eines Darmcarcinoms die Berechtigung zu einer Probeincision geben, durch welche die weitere Diagnose und die Art der vorzunehmenden Operation erst entschieden werden muss. Insofern ist eine praecise Differentialdiagnose des Grundleidens vor der Operation von geringer praktischer Bedeutung. Dagegen müssen wir in einer Richtung die klinischen Erscheinungsformen des Darmcarcinoms streng auseinanderhalten, nämlich je nachdem es unter dem Bilde des acuten Ileus oder aber der chronischen Darmstenose, resp. anderer mehr schleichender Symptome in unsere Behandlung kommt. Auf diesen Punkt haben schon mehrere erfahrene Chirurgen, zuletzt Koerte hingewiesen; es wird aber immer noch nicht als allgemein gültige Regel angesehen, einen Fall von Darmcarcinom mit acutem Ileus und einen solchen (p. 36) ohne Ileus als zwei Krankheiten anzusehen, die nicht nur prognostisch verschieden zu beurtheilen, sondern auch in Bezug auf die operative Therapie verschieden zu behandeln sind. Der Kranke mit einem unter chronischen Erscheinungen verlaufenden Darmcarcinom ist selbst, wenn er in seiner Ernährung recht herunter gekommen ist, falls nicht schon ausgedehnte Metastasen, Ascites oder vorgeschrittene Kachexie vorhanden ist, in der Regel widerstandsfähig genug, um einen schwereren Eingriff, zumal die Radicaloperation zu vertragen. Die Hauptgefahr, die der peritonealen Infection, können wir durch die später zu besprechende zweizeitige Resectionsmethode fast mit Sicherheit vermeiden. Demgegenüber ist ein Carcinomkranker mit acutem Ileus nach jeder Richtung hin sehr wenig leistungsfähig. Einer grossen intraabdominellen Operation, selbst einer technisch noch so günstig gelegenen Darmresection, ist er meist nicht mehr gewachsen. Es würde zu weit führen, hier alle Gründe dafür anzuführen. Die Statistik zeigt, dass Ileuskranken Eingriffen, welche die Kranken der ersten Kategorie spielend überstehen, meist erliegen. Nur ausnahmsweise gelingt es einmal, einen derartigen Kranken nach der Resection durchzubringen. Die 3 von mir operirten Fälle sind sämmtlich gestorben. (Einer hatte allerdings die Hauptoperation, den ersten Akt der zweizeitigen Resection, glücklich überstanden und starb erst an einer Nachoperation). Selbst die Enteroanasto-

mose wird meist ein zu schwerer Eingriff sein. Wir werden uns daher bei Ileus wegen Darmcarcinoms auf das nothwendige Minimum des Eingriffes beschränken, d. h. zunächst nur die Colostomie ausführen, und sofern der Tumor zur Resection geeignet ist, dieselbe erst in einer zweiten Sitzung, nachdem der überstaute, in seiner Ernährung schwer geschädigte Darm sowie der Patient sich vollständig erholt haben, vornehmen.

Nach dem Gesagten bedarf es keiner weiteren Begründung, wenn ich von meinen 106 Fällen 23, welche mit acutem Ileus der Klinik zugeführt wurden, von den übrigen 83 sondere. Unter den letzteren befinden sich auch solche die früher ausserhalb der Klinik an acutem Ileus erkrankt waren und nach erfolgreicher Colostomie bei uns einer zweiten Operation unterzogen wurden.

Beschäftigen wir uns zunächst mit den letzteren Fällen, die mit chronischen Symptomen in unsere Behandlung kamen. Bekanntlich (p. 37) stehen uns hier neben der Resection, als Palliativoperationen noch zur Verfügung: die einfache Colostomie und die Enteroanastomose mit completer oder incompleter Darmausschaltung. Nicht immer werden wir in der Lage sein, von vornherein zu bestimmen, ob die Radicaloperation möglich sein wird, oder ob wir uns auf eine der Palliativoperationen beschränken werden. In diesem Falle wird die Operation als Probeincision zu beginnen haben. Ueber die Grundsätze, welche uns bei der Wahl zwischen Radicaloperation und einer der palliativen Operationen leiten sollen, sobald einmal die Bauchhöhle eröffnet ist, sind wir im Allgemeinen einig. Immerhin wird es im einzelnen Falle noch sehr von der persönlichen Erfahrung abhängen, ob der Operateur sich noch zu der eingreifenden Radicaloperation oder zu einer Palliativoperation entschliesst, oder ob er gar die Bauchhöhle unverrichteter Dinge wieder schliesst. Früher, als ich in der Regel die einzeitige Resection übte, entschloss ich mich nur bei günstigen allgemeinen und lokalen Bedingungen zur Resektion. Seit ich die ungleich weniger gefährliche zweizeitige Methode übe, gehe ich viel weiter. Selbstverständlich wird, wenn wir in der Indicationsstellung noch so weit gehen, immer eine nicht unbeträchtliche Zahl von Fällen übrig bleiben, bei denen wir von jeder Operation absehen.

Die 83 Fälle von malignem Darmtumor mit chronischen Symp-

tomen vertheilen sich nach der Art der eingeleiteten Behandlung folgendermaassen:

Nicht operirt.....	17 ¹
Probeincision.....	7 davon + 0
Colostomie.....	6 davon + 0
Enteroanastomose mit Darmausschaltung.....	16 davon + 3
Resection.....	37 davon + 11
= + 29,7 pCt.....	
Davon einzeitig mit primärer Naht.....	21 davon + 9
= + 42,9 pCt.....	
Zweizeitig mit Vorlagerung.....	16 davon + 2
= + 12,5 pCt.....	

(p. 38) In Bezug auf die unmittelbaren Resultate der einfachen Probeincision und der Palliativoperationen ist nichts Besonderes zu bemerken. Dagegen lohnt es sich, näher auf die Erfolge der Radicaloperation einzugehen. Es fällt ohne Weiteres die grosse Ueberlegenheit der zweizeitigen Resektionsmethode über die einzeitige mit primärer Darmnaht in die Augen. Bei dieser eine Mortalität von 42.9 pCt., bei jener nur 12.5 pCt. Das Resultat erscheint noch günstiger, wenn wir berücksichtigen, dass die zwei Todesfälle bei der zweizeitigen Methode nicht der Operation als solcher zur Last fallen. Ein Fall starb 7 Wochen nach der Operation an Marasmus infolge von Carcinommetastasen; im zweiten Falle war Peritonitis die Todesursache und zwar infolge der Ruptur des carcinomatös infiltrirten Colon descendens, welches mit dem Colon transversum verwachsen war und bei der Ablösung einriss.

Soweit ich in der Literatur orientirt bin, gilt heute fast allgemein noch die einzeitige Resektion des carcinomatösen Darmes mit primärer Darmnaht als Regel. Die Resultate dieser Operation sind nun gerade beim Carcinom im Bereiche des Dickdarms bisher recht wenig befriedigend, gleichgiltig, ob die Darmvereinigun- gung nach der alten Methode durch circuläre Darmnaht oder durch seitliche Implantation oder Apposition oder endlich mit dem Darmknopf bewerkstelligt wird. Ich brauche nur einige

¹ Davon ein Fall noch in der Klinik gestorben. Die Operation wurde in der Regel wegen zu weit fortgeschrittener Cachexie, wegen Metastasen u.s.w. unterlassen. Etliche Male verweigerte der Patient die vorgeschlagene Operation.

statistische Zahlen anzuführen. Von Koerte's 19 radikal operirten Fällen starben 7 (3 davon allerdings im Ileus operirt), von Czerny's 18 Fällen starben 9, von v. Bramann's 14 Fällen 6, von Kroenlein's 12 Fällen 6. Mit diesen Zahlen stimmt so ziemlich überein die grosse Statistik von de Bovis, welcher 104 Fälle aus zusammenhängenden Serien bekannter Chirurgen zusammengestellt hat. Die Mortalität beträgt 38.4 pCt. De Bovis hat ferner 51 Todesfälle nach der einzeitigen Resection auch aus anderen Einzelpublikationen zusammengestellt. 13 mal war Collaps, 30 mal Peritonitis die Todesursache. Interessant ist auch die Thatsache, dass bei den ohne Drainage der Peritonealhöhle Nachbehandelten die Mortalität $\frac{1}{3}$ höher war als in den drainirten Fällen. Die angeführten Zahlen sprechen deutlich genug. Die Todesfälle an Collaps beweisen, dass die Operation für einen beträchtlichen Theil der Patienten zu eingreifend war. Die 30 Fälle von Peritonitis beweisen, dass in mehr als der Hälfte der Todesfälle das Peritoneum (p. 39) entweder noch während der Operation inficirt wurde, oder die Peritonitis nachträglich durch Insufficienz der Naht entstand. Zweifellos ist die Gefahr der peritonealen Infection bei dieser Operation, sei es primär, sei es secundär durch Insufficienz der Naht, enorm gross. Das ist leicht verständlich, wenn wir uns die Verhältnisse vergegenwärtigen, unter welchen die Darmnaht vorgenommen wird. Die Darmvereinigung am Dickdarm—von diesem allein sprechen wir hier—ist an und für sich wenig verlässlich, nach welcher Methode wir sie auch immer vornehmen mögen. Die geringere Stärke der Dickdarmwand, die schlechtere Gefässversorgung, die träge Peristaltik, infolge deren der eingedickte Koth an der Nahtstelle stagnirt, geben lange nicht die Sicherheit für die primäre Verklebung an der Nahtstelle wie beim Dünndarm; dazu kommt, dass wir beim Darmcarcinom in der Regel nicht normale Darmtheile mit einander vereinigen. Der zuführende Schenkel ist häufig überdehnt und infolge dessen schlecht ernährt, häufig ist er auch paretisch, wodurch die Stagnation und die Unsicherheit der Naht noch gesteigert wird. Viel höher, als im Allgemeinen angenommen wird, ist die Gefahr der primären Infection des Peritoneums durch den eröffneten Darm anzuschlagen. Wenn wir auch noch

so peinlich durch temporäre Tamponade das zu rescirende Darmstück von der Peritonealhöhle ausschalten, die Verbreitung von Darmbakterien auf der Serosa selbst in weiter Entfernung lässt sich dabei doch nicht verhindern. In einer interessanten Arbeit hat Hans Buchbinder¹ nachgewiesen, dass selbst aus einer feinsten Stichöffnung des Darms sich die Bakterien mit grosser Geschwindigkeit auf der Oberfläche der Serosa verbreiten und zwar nicht nur auf die unmittelbar betroffenen, sondern auch auf die benachbarten Darmschlingen. Wir müssen demnach damit rechnen, dass bei jeder Magen- und Darmoperation trotz aller Kautele Bakterien in einer gewissen Menge in die Peritonealhöhle gelangen. Je länger die Operation dauert, desto grösser die Menge derselben. Nun wird zweifellos in vielen Fällen, wir können fast sagen in der Regel, vom Peritoneum ein geringes Maass von Bakterieninvasion überwunden; der Effekt ist die nach allen Magen- und Darmoperationen beobachtete circumscripte Peritonitis, die zu den z. Th. schützenden (p. 40) Verlöthungen in der Umgebung der Nahtstelle führt. Die Fähigkeit, eine derartige geringfügige peritoneale Infektion glücklich zu überwinden, hängt nun in erster Linie von der Widerstandsfähigkeit des ganzen Organismus ab. Der an acutem Ileus Erkrankte ist infolge der Darmintoxication so widerstandslos, dass er selbst ein Minimum von Infection nicht überwindet. Aber auch bei der chronischen Darmstenose, die ja, wie wir wissen, in der Regel das Darmcarcinom begleitet, befindet sich der Patient im Zustande einer chronischen Intoxication, durch die er den Darmbakterien gegenüber zweifellos auch weniger widerstandsfähig wird. Wir finden darin eine genügende Erklärung für die schlechten Resultate der einzeitigen Darmresektion bei Carcinom. Ich zweifle nicht, dass auch die häufigen Pneumonien nach diesen Operationen z. Th. wenigstens auf eine bakterielle Infection vom Peritoneum aus zurückzuführen sind, die lokal wohl glücklich überstanden wird, aber auf dem Wege kleiner Lungenembolien zur Pneumonie führt.

Es ist somit kein Zweifel, dass wir eine Besserung der Resultate nur erzielen können, wenn wir

¹ Experimentelle Untersuchungen am lebenden Thier- und Menschendarm. Deutsche Zeitschrift für Chirurgie. Bd. 55. S. 458.

1. die Operation weniger angreifend gestalten und dadurch die Gefahr des Collapses verringern, und

2. die peritoneale Infection während der Operation und im Verlaufe der Heilung verhindern. Beides erreichen wir durch die zweizeitige Operation.

Die Idee, die Darmcarcinome durch zweizeitige Operation zu entfernen, ist keineswegs neu. Noch Ende der 70. Jahre sahen sich Schede, Gussenbauer, Maydl, v. Volkmann u. A. theils durch die technische Unmöglichkeit, nach der Resection des Tumors die Darmenden durch die Naht zu vereinigen, theils weil der Kräfteverfall des Kranken eine rasche Beendigung der Operation verlangte, gezwungen, dieselbe mit der Anlegung eines Anus praeternaturalis zu beschliessen. Dieser konnte, wenn die Verhältnisse es gestatteten, nachträglich geschlossen werden. Neben dieser durch die Nothlage gegebenen zweizeitigen Operation wurden später auch andere Combinationen verwendet, so zunächst Anlegung eines Anus praeternaturalis oberhalb der stenosirten Stelle, zumal wenn Ileus bestand, in einer späteren Zeit die Resection mit typischer Darmnaht. Eine allgemein bekannte Combination ist ferner: zunächst Enteroanastomose mit partieller oder totaler Ausschaltung (p. 41) des erkrankten Darmstückes und in einer späteren Sitzung Exstirpation des Tumors. Die zwei letztgenannten Combinationen haben zweifellos den grossen Vorthail, dass sie zunächst den zuführenden Darm entlasten und dadurch die secundären Veränderungen an demselben beseitigen. Die zweite Operation wird dann innerhalb annähernd normaler Darmtheile vorgenommen. Eine der Hauptgefahren aber beseitigen diese zwei Combinationen gar nicht oder nur in unzureichendem Maasse, nämlich die der primären und secundären Infection des Peritoneums. Diese Gefahr nebst allen anderen wird am besten umgangen durch die zweizeitige Operation, wie ich sie seit nunmehr 5 Jahren principiell bei allen Dickdarmtumoren ausübe. Sie besteht im Wesentlichen darin, dass der Tumor wie zur einzeitigen Resection aus allen seinen Verbindungen gelöst wird bis auf den Zusammenhang mit dem zu- und abführenden Darmschenkel. Der so mobil gemachte Tumor wird vor die Bauchwunde gelagert, diese bis auf die Durchtritt-

stelle der beiden Darmschenkel verschlossen und nun entweder sofort oder nach Ablauf von 12–48 Stunden der Tumor extraperitoneal reseziert. Der resultirende Anus praeternaturalis wird später verschlossen.

Dem Princip nach wurde dieses Verfahren meines Wissens zuerst von Oscar Bloch in Kopenhagen im Jahre 1892 angewandt. Er fand in einem Falle von Ileus als Ursache desselben einen frei beweglichen, in der Flexura sigmoidea sitzenden Tumor. Er lagerte denselben sammt dem langen Mesosigmoideum vor die Bauchwand und incidirte den Darm oberhalb der Geschwulst. Nach Beseitigung der Ileuserscheinungen führte er extraperitoneal die Resection aus, welcher nach 4 Monaten der Verschluss des Anus praeternaturalis durch die circuläre Darmnaht folgte. Bloch empfahl dieses Verfahren zunächst nur für Darmtumoren mit beweglichem Mesenterium und sprach auch schon damals die Ueberzeugung aus, dass die meisten Gefahren der Operation durch die extraabdominelle Darmresection beseitigt würden. Zwei Jahre später ging er einen Schritt weiter, indem er einen wenig mobilen Tumor des Colon descendens dadurch genügend mobilisirte, dass er die Umschlagstelle von Gekröswurzel und Peritoneum incidirte. Ob Bloch später noch weiter gegangen ist und in der von mir geübten Weise vorging, indem er auch das Mesenterium primär resezirte, ist mir nicht bekannt. Jedenfalls lag die Idee dazu nicht fern. (p. 42) Es ist klar, dass das ursprüngliche Bloch'sche Verfahren, abgesehen von seiner beschränkten Anwendbarkeit den grossen Nachtheil hat, dass durch die Belassung des Mesenteriums die regionären Lymphdrüsen unberücksichtigt bleiben. Ausser Bloch haben später noch andere Chirurgen in vereinzeltten Fällen ein ähnliches Verfahren eingeschlagen. So Allingham, W. Edmunds, Hochenegg u. A. Im Ganzen finde ich bei De Bovis 8 derartige Operationen verzeichnet, die alle mit günstigem Erfolge endeten. Dass von meinen 16 Fällen nur 2 tödtlich verliefen und dass in beiden Todefällen die Operationsmethode an dem unglücklichen Ausgange nicht schuld war, habe ich schon früher erwähnt. Die Operation, wie sie in meiner Klinik im Laufe der letzten Jahre ausgebildet worden ist, gestaltet sich des Genaueren folgendermaassen.

Es wird der Darmtumor sammt den erkrankten Lymphdrüsen und dem entsprechenden Stück Mesenterium wie bei der einzeitigen Resection aus allen Verbindungen gelöst, sodass er schliesslich nur noch mit dem zu- und abführenden Darm in Verbindung steht. Die Ablösung des Mesenteriums muss soweit geschehen, dass der zu exstirpirende Darmabschnitt ohne stärkere Spannung vor die Bauchwand gelagert werden kann. Ist dies geschehen, so wird die Bauchwand soweit geschlossen, dass nur der zum Durchtritt des zu- und abführenden Darmschenkels nöthlige Spalt freibleibt; dieser Spalt darf nicht zu eng sein, damit der zuführende Darmschenkel nicht comprimirt wird. An der Berührungsstelle des Peritoneum parietale mit den heraustretenden Darmschenkeln wird eine Reihe von Serosanähten angelegt, die die Peritonealhöhle auch an dieser Stelle abschliessen. Die äussere Haut wird bis an die heraustretenden Darmschenkel exact vernäht (keine Tamponade). Nun wird die Nahtlinie sowie die Berührungsfläche zwischen vorliegendem Darm und Hautwunde dick mit Zinkpaste bedeckt und darüber steriles Verbandzeug gelegt. Ueber den Wundverband kommt noch ein grösseres Stück wasserdichten Stoffes mit einem Schlitz gerade gross genug, den vorgelagerten Darm heraustreten zu lassen. So ist schliesslich der zu resecirende Tumor von der Bauchhöhle nicht nur durch die vernähten Bauchdecken, sondern auch durch den schützenden Verband getrennt. Früher habe ich den Tumor erst nach Ablauf von 12–48 Stunden abgetragen, jetzt thue ich est meist sofort. In den abführenden Darmschenkel (p. 43) wird ein dickes Glasrohr eingebunden und an dieses ein dickes Gummirohr befestigt, durch das der Darminhalt nach aussen abfliesst.

Die Bauchdeckenwunde heilt bei diesem Vorgehen soweit sie vernäht ist, anstandslos per primam. Den bei der Abtragung des Tumors resultirenden widernatürlichen After verwandle ich nach 2–3 Wochen mittels meiner Sporenquetsche zunächst in eine Kothfistel, die später durch Naht verschlossen wird.

Die Vortheile dieses Verfahrens sind ersichtlich. Die Hauptoperation ist kürzer als bei der einzeitigen Methode, die Infection des Peritoneums während der Operation wird absolut vermieden, man kann sie daher einem durch das Leiden heruntergekommenen Kranken viel eher zumuten. Ein weiterer Vortheil ist der, dass

man sie bei weiter Ausdehnung des Tumors oder bei tiefem Sitze, z. B. am unteren Schenkel der Flexura sigmoidea auch in solchen Fällen ausführen kann, in welchen die primäre Darmnaht wegen zu starker Spannung der zu vereinigenden Darmschlingen zu gewagt wäre. Die Methode ist also nicht nur ungefährlicher, sondern auch leistungsfähiger. Allerdings hat das Verfahren auch seine Schattenseiten. Die Behandlungsdauer ist eine viel längere und der Operirte muss eine Zeit lang die Unannehmlichkeiten eines widernatürlichen Afters über sich ergehen lassen. Aber das sind, denke ich, Nachtheile, die durch den Vortheil der grösseren Sicherheit und Leistungsfähigkeit reichlich aufgewogen werden.

Ich stehe demnach nicht an, das geschilderte Verfahren der zweizeitigen Darmresection als die Normalmethode bei allen Fällen von Tumoren des Dickdarms zu empfehlen, auch wenn keinerlei Complicationen vorliegen. Beim Dünndarm verwende ich, falls nicht acuter Ileus vorliegt, die einzeitige Resection mit primärer Darmnaht. Die Tumoren des Coccums sehe ich als Grenzfälle an. Ich mache es vom Kräftezustand des Kranken, von der Beschaffenheit des zuführenden Darmes, von den grösseren oder geringeren technischen Schwierigkeiten bei der Freipräparirung des Tumors abhängig, ob die primäre Naht angeschlossen wird oder nicht. Bleibt nach Auslösung des Tumors, was gewöhnlich der Fall ist, eine breite, des Peritoneums entbehrende Wundfläche zurück, so dass ein grösserer toter Raum entsteht, so gehe ich auch hier zweizeitig vor.

(p. 44) Gestatten Sie mir, meine Herren, noch in Kürze auf die Dauerresultate bei meinen Operirten einzugehen. In erster Linie interessiren uns die Endresultate der Radicaloperation. Die Operationsmethode, ob ein- oder zweizeitig, giebt hierbei keinen Ausschlag. Ich darf daher die einzeitig und zweizeitig operirten Fälle zusammenfassen. Vorliegende Tabelle giebt Ihnen Aufschluss über die späteren Schicksale von 20 Operirten, über die wir sichere Nachrichten hatten.

Radicaloperation

37 Fälle, davon 11. Ueberlebend: 26 Fälle. Keine Nachricht erhalten von 6 Fällen [2 davon mit Recidiv entlassen.]

Es bleiben somit 20 Fälle. Von diesen sind:

1. + an Recidiv: 9 Fälle u. zw.

- 1 Fall nach $5\frac{1}{2}$ Jahr
- 1 Fall nach $14\frac{1}{3}$ Monaten
- 1 Fall nach 13 Monaten
- 1 Fall nach 11 Monaten
- 1 Fall nach 8 Monaten
- 1 Fall nach 7 Monaten
- 1 Fall nach 6 Monaten
- 1 Fall nach $5\frac{1}{2}$ Monaten
- 1 Fall nach $3\frac{1}{2}$ Monaten

Summa 9 Fälle, durchschnittliche Lebensdauer nach der Operation 15 Monate.

2. Es lebt mit Recidiv: 1 Fall nach 13 Monaten.

3. Es leben recidivfrei: 10 Fälle u. zw.

- 1 Fall $9\frac{1}{4}$ Jahre
- 1 Fall $5\frac{3}{4}$ Jahre
- 1 Fall $4\frac{3}{4}$ Jahre
- 1 Fall $4\frac{1}{4}$ Jahre
- 1 Fall 4 Jahre
- 1 Fall 2 Jahre
- 1 Fall $1\frac{1}{2}$ Jahre
- 1 Fall $1\frac{1}{4}$ Jahre
- 2 Fälle $\frac{1}{4}$ Jahre

(p. 45) Die Operation liegt länger als 4 Jahre zurück bei 12 Fällen, welche die Operation überstanden. Von diesen sind 5 als radical geheilt anzusehen.

Wie Sie sehen, ist das Endresultat, wenn wir eine Recidivfreiheit von 4 Jahren als Dauerheilung ansehen, ein sehr erfreuliches. Dass nach der Resection von Darmcarcinomen wirklich Dauerheilungen vorkommen, die ein Jahrzehnt und darüber anhalten, ist ja längst erwiesen. Ich brauche nur die bekannten Fälle von Gusserbauer-Martini, v. Bergmann, Rehn, v. Bramann, Czerny, Kroenlein, Frank, Hochenegg, Lilienthal, Koerte anzuführen. Auch ein Fall aus meiner früheren Beobachtungszeit ist 16 Jahre recidivfrei geblieben. Solche Einzelbeobachtungen geben uns allerdings noch keinen Aufschluss über die Aussichten auf Radicalheilung, auf die wir im einzelnen Falle rechnen können.

Dies werden vielleicht später ausgedehntere statistische Zusammenstellungen ermöglichen. Aber auch schon die jetzigen Erfahrungen berechtigen uns zu den schönsten Hoffnungen. In dem Berichte von Koerte finde ich unter den 12 Fällen, bei welchen die Operation auch mindestens 4 Jahre zurückliegt, 4, welche recidivfrei geblieben sind. Mit meinen Zahlen zusammengekommen gäbe das 24 Fälle mit 9 Dauerheilungen = 37,5 pCt.

Ueber die Enderfolge der Palliativoperationen bei Darmcarcinom geben folgende zwei Tabellen Aufschluss.

Colostomie

Es haben gelebt:

A. Seit Beginn der Erkrankung.

1 Fall, 6½ Jahre

1 Fall, 4½ Jahre

3 Fälle, 3¾ Jahre

1 Fall, 2¾ Jahre

1 Fall, 2½ Jahre

1 Fall, 2¼ Jahre

1 Fall, 2 Jahre

Durchschnittl.: 3 J. 6 Mon.

B. Seit der Operation.

1 Fall, 4½ Jahre

1 Fall, 3¼ Jahre

1 Fall, 2¾ Jahre

2 Fälle, 2 Jahre

1 Fall, 1¼ Jahre

1 Fall, 10 Monate

1 Fall, 5 Monate

1 Fall, 2½ Monate

1 Fall, 1½ Monate

Durchschnittl.: 1 J. 9 Mon.

Enteroanastomose

(p. 46) A. Seit Beginn der Erkrankung.

1 Fall, 3½ Jahre

1 Fall, 2 Jahre

1 Fall, $1\frac{1}{2}$ Jahre

1 Fall, $1\frac{1}{4}$ Jahre

2 Fälle, 11 Monate

1 Fall, 7 Monate

Durchschnittl.: 1 J. $6\frac{1}{3}$ Mon

B. Seit der Operation.

1 Fall, $9\frac{1}{2}$ Monate

1 Fall, 9 Monate

3 Fälle, 7 Monate

1 Fall, $6\frac{1}{2}$ Monate

1 Fall, $4\frac{1}{2}$ Monate

1 Fall, $1\frac{1}{4}$ Monate

Durchschnittl.: $8\frac{1}{2}$ Mon

Auffallend ist die lange Lebensdauer einzelner Fälle nach der Colostomie. Wir haben bei diesen Kranken versucht ausser der Lebensdauer nach der Operation noch die Lebensdauer seit Beginn der ersten Krankheitserscheinungen festzustellen, um uns daraus ein Bild in Bezug auf die Lebensdauer der Darmcarcinomkranken überhaupt zu machen.¹ Wie Sie sehen, finden wir auch hierbei auffallend hohe Zahlen, welche mit der bisherigen Annahme in Bezug auf die Lebensdauer beim Darmcarcinom nicht übereinstimmen. Dieselbe wurde bisher allgemein entschieden zu niedrig veranschlagt. Zur Vervollständigung haben wir uns auch über das weitere Schicksal der nicht operirten oder nur einer Probeincision unterworfenen Kranken zu unterrichten gesucht. Die Zahlen sind hier, wie Sie aus beifolgender Tabelle ersehen, viel ungünstiger.

Nicht operirte Fälle und Probencisionen

Es haben gelebt seit Auftreten der ersten Erscheinungen:

1 Fall, 20 Monate

1 Fall, 18 Monate

1 Fall, 17 Monate

¹ Die Gesamtzahl der unter A. angeführten Fälle ist sowohl bei der Colostomie als auch bei der Enterostomie kleiner als unter B., weil nicht in allen Fällen der Beginn der Erkrankung genügend festzustellen war.

1 Fall, 12 Monate

2 Fälle, 9 Monate

1 Fall, 8 Monate

1 Fall, 3 Monate

Durchschnittlich: 12 Monate

Offenbar waren es von Haus aus malignere, rascher wachsende Carcinome, die sich eben deshalb zu einer Operation nicht eigneten.

(p. 47) In Bezug auf die Erfolge der Operation bei Ileus infolge von Darmcarcinom kann ich mich ganz kurz fassen, da die einschlägigen Beobachtungen in einer späteren Mittheilung aus meiner Klinik über Ileus noch eingehender besprochen werden sollen. Von 23 Fällen, die mit acutem Ileus in die Klinik kamen und operirt wurden, genasen 12 vom Ileus; 11 starben. Auffallend ist der Unterschied in der Prognose je nach dem Sitze des obturirenden Carcinoms; je höher es liegt, desto ungünstiger die Prognose. 14 mal sass der Tumor in der Flexura sigmoidea, nur 3 von den Operirten starben, während von den 9 Kranken mit höherem Sitze des Carcinoms 8 zu Grunde gingen. Ferner zeigt sich an unserem wenn auch kleinen Material, dass die Prognose um so besser ist, je geringfügiger der vorgenommene Eingriff. Von 15 Fällen, in welchen nur ein Anus praeternaturalis angelegt wurde, starben nur 4. 10 mal sass das Carcinom in der Flexura sigmoidea, von den Fällen starb nach der Colostomie nur 1. Von 5 Patienten mit höherem Sitze des Tumors starben 3. Die 2 Fälle, in welchen die Enteroanastomose vorgenommen wurde, starben beide, ebenso 5 Fälle, in welchen die Resection ausgeführt wurde.

Nach diesen Erfahrungen ist es begreiflich, dass ich es mir zum Grundsatz gemacht habe, bei Ileus wegen Darmcarcinom in der Regel mich auf die einfache Colostomie zu beschränken. Ich würde nun ausnahmsweise, wenn die Verhältnisse besonders günstig liegen, die zweizeitige Resection vornehmen. Die einfache Colostomie hat neben anderen noch den enormen Vortheil, dass wir sie unter localer Anaesthesie vornehmen können. Der Eingriff wird dadurch fast ganz ungefährlich. Die Vornahme der Colostomie unter localer Anaesthesie setzt allerdings voraus,

dass wir den Sitz des Hindernisses mit annähernder Sicherheit vorausbestimmen können. Dies ist mit unseren heutigen diagnostischen Hilfsmitteln in der grossen Mehrzahl der Fälle möglich. Ist trotzdem ein Irrthum untergelaufen und hat man z. B. einen Schnitt zum Anus sigmoideus angelegt, ohne daselbst die geblähte Darmschlinge zu finden, so wird man durch eine zweite Incision unter localer Anaesthesie in der Ileocoecalgegend dem Kranken gewiss viel weniger schaden, als wenn man in Narkose die Bauchhöhle breit eröffnet und erst nach dem Hindernis sucht.



Surgical Experiences with Intestinal Carcinoma¹

BY

J. VON MIKULICZ

in Breslau

THE surgical treatment of intestinal carcinoma has been repeatedly the object of much detailed discussion in our Society. I need only recall the very instructive report of Mr. Koenig in 1890, the communications of Mr. von Bramann in 1898 and the exhaustive presentation of Mr. Koerte, who, some two years ago, was able to report on 54 pertinent cases. In the same year DeBovis, in the *Review of Surgery*, gave a critical compilation of approximately 450 cases of intestinal carcinoma which had been treated surgically, together with a well prepared review of the experiences recorded in the literature. It will therefore appear almost superfluous to bring the subject up again for discussion. And yet every surgeon must be convinced of the fact, by his own experiences as well as by a perusal of the literature, that we are still at some distance from a solution of the whole problem. Even if today we can say that intestinal carcinoma offers one of the most satisfactory fields of abdominal surgery, our results leave much to be desired. They must be improved by a perfection of the technique; they must also be improved by an exhaustive study of the clinical phenomena of intestinal carcinoma; for by this means we will be enabled to

¹ Discourse presented at the 31st Congress of the German Society of Surgery. Published in *Arch. f. klin. Chir.*, 69: 28-47, 1903.

recognize the malady earlier and to undertake surgical treatment in an earlier stage. Perhaps my modest experiences will offer a small contribution thereto.

During the course of the last eleven years, 106 cases of malignant intestinal tumors—with the exception of those of the rectum—have come under observation in the Breslau clinic. Five of these were sarcoma, three of the small intestine, and two of the large. One presented an endothelioma of the transverse colon. One hundred times it was a question of carcinoma; of these five occurred in the small intestine and 95 in the large bowel.

Since intestinal sarcoma in most cases presents the same clinical picture as intestinal carcinoma, in the following discussion I take the liberty of considering the two tumor forms as one for all practical purposes.¹

According to sex, 80 cases were in men and 26 in women. Such a marked preponderance in the male sex (3:1) to my knowledge has not been presented in the other statistics. According to DeBovis the ratio of male to female is 54:46.

In reference to age, all periods from the second to the eighth decade of life are represented in my series. The youngest patient was 16 years of age. The following table shows the distribution of cases according to age.

Age	Males	Females	Total
Under 20	—	1	1
20-29	3	1	4
30-39	10	5	15
40-49	19	3	22
50-59	23	10	33
60-69	21	6	27
70-79	3	—	3
Over 80	1	—	1

¹ The striking differences in the clinical courses of intestinal sarcoma and intestinal carcinoma which occasionally occur, namely the rapid growth and the complete lack of the phenomena of stenosis in sarcoma, are to be made use of in the differential diagnosis of the single case only with extreme caution, since we also observe the greatest difference in both directions in the various forms of intestinal cancer. A detailed discussion is to be found in the chapters of the third volume of the Handbook of Practical Surgery by v. Bergmann, v. Bruns and v. Mikulicz.

According to the level of intestinal segment affected, the tumors were distributed in the following manner:

- a) Small intestine 8 cases (5 carcinoma, 3 sarcoma).
- b) Cecum 20 cases (19 carcinoma, 1 sarcoma).
- c) Colon (with exception of cecum and sigmoid flexure) 40 cases as follows:
 - a) Ascending colon: 6 cases.
 - b) Hepatic flexure: 7 cases.
 - c) Transverse colon: 8 cases.
(7 carcinoma, 1 endothelioma)
 - d) Splenic flexure: 12 cases.
 - e) Descending colon: 4 cases.
 - f) Colon without exact localization: 3 cases.
- d) Sigmoid flexure: 31 cases.
- e) Point of origin unknown¹ 7 cases (1 sarcoma, 6 carcinoma).

The figures given coincide well with the other statistics, which are for the most part more extensive, in that they show that the most common site of predilection for intestinal carcinoma is the sigmoid flexure and the next most common is the cecum.

Although the distribution of intestinal carcinoma in the various portions of bowel is so regular, the clinical course in individual cases is without any standard rule at all, if we disregard the fact that the height of the affected section of gut exerts a certain influence on the development of the clinical phenomena. It is well known that a tumor which has once produced outspoken functional disturbances in the intestine, runs a different course according to whether it is in the small bowel, cecum or in the lower portion of the large bowel. In general it may be said that the higher the intestinal cancer, the more pregnant the phenomena and the more stormy the disturbances. But disregarding the location, an intestinal cancer at one and the same spot can in one case remain completely latent for a long period, at another time produce vague intestinal symptoms, a third time the symptoms of chronic stenosis and a fourth time acute

¹The cases of indefinite localization refer to patients not operated on, in whom the diagnosis could be made by the clinical findings, and a few times, as in one case of intestinal sarcoma, on the basis of extirpated lymph nodes.

ileus. We need not wonder over the variability of the course if we but consider that an intestinal tumor produces no symptoms of itself alone, since it is established in an organ which, as we know, has no sensory nerves. The effect on peristalsis as a result of the infiltration of a limited segment of intestinal wall is also of no significance, for the passage of the products of digestion, as the adjacent portion of gut above is powerful enough to act vicariously for the section of intestine not capable of peristalsis. Only through complications does cancer of the intestine become clinically noticeable. These are stenosis, ulceration and hemorrhage. The last two complications are as a rule made manifest only in carcinomas situated low down, in the region of the flexures and the descending colon, by the admixture of blood and pus with the stools; bleeding in higher locations, if profuse, is a rare occurrence in intestinal cancer, as is well known. We must regard stenosis as the most constant complication which sooner or later enters into almost every case, but we unfortunately know it is not an early symptom. Probably most carcinomas produce stenosis in the anatomical sense very quickly, but for a long time this need not lead to stenosis in the clinical sense, that is, the prevention of passage of contents at the affected area. The section of gut lying above the stenosis compensates for a long time as the result of a constantly increasing hypertrophy, and, indeed, this may be so complete that no functional disturbances need become evident. To what extent this hypertrophy can go is best shown in those cases where a former apparently healthy person is suddenly stricken with acute ileus, as the cause of which there is found an intestinal cancer already possessing a marked degree of stenosis. Clinically, stenosis occurs when severe symptoms of intestinal catarrh develop as the result of continued congestion above the carcinoma, when insufficient passage through the stenosed area of the bowel leads to forceful, cramp-like peristalsis (rigid bowel), or when by a chance occurrence (foreign body, inflammatory swelling) the narrowed spot suddenly becomes wholly impassable. At this point I need not go further into the well known symptoms of chronic intestinal stenosis or acute occlusion of the gut. I should like to stress

the fact, though, that intestinal carcinoma commonly can remain symptomless over a long period of time or run an atypical course, so that one should also include carcinoma in the differential diagnosis of apparently insignificant disturbances of intestinal function, especially when the phenomena occur in an elderly person who has previously enjoyed faultless digestion. Occasionally, by means of a thorough examination of the abdomen, inflation of the bowel and other methods of investigation, a palpable tumor or other indications of intestinal tumor are found long before severe functional disturbances occur.

Moreover I assume it is known that the histologic structure of the carcinoma exerts a definite effect as to whether a marked degree of stenosis develops early or late. In this respect the contrasts are striking between the clinical manifestations of large extensive tumors and small tumors not at all palpable through the abdominal wall. A large, relatively soft, extensive, ulcerating tumor which maintains the intestinal lumen can run its course without much hindrance to the intestinal passage, while a small scirrhus cancer, limited to a few centimeters, can cause severe symptoms of stenosis very early because of the firm contraction. Carcinoma of the latter type are common in the region of the sigmoid flexure.

Perhaps it would not be unsuitable to classify intestinal carcinomas in various types according to their clinical course or the stages passed through in the single case, as, for example, DeBovis does in differentiating three types:

1. Type of absolute or relative latency.
2. Gastrointestinal type.
3. Type of severe occlusion.

This preliminary arrangement certainly has qualifications, since most cases pass through at least two and perhaps all three stages, one after the other.

From another and more practical point of view, I should like to differentiate the following three periods in the course of intestinal carcinoma.

- A) Latent period.
- B) Period of initial symptoms.

C) Period of clinically demonstrable symptoms.

A) In regard to the latent period, it is self-evident that we can only state suppositions. Observations made later when a palpable abdominal tumor presents in a striking way as the first symptom of an intestinal cancer or cases in which an acute ileus suddenly occurs as the result of an intestinal tumor, without any prodromal symptoms, indicate that intestinal carcinoma can exist latently for a long period, at any rate much longer than is commonly assumed. Also the observation that a patient with intestinal cancer may live for some years in relatively good health following colostomy (in a case under my observation four and one-half years), speaks in a like manner. These observations also show that intestinal carcinoma, contrary to the view of most clinicians, is a relatively benign carcinoma, because glandular metastases and metastases to other organs in many cases do not occur until late. We must call special attention to this because it speaks highly for the appropriateness of operative therapy in intestinal cancer, a fact which at present is all too little recognized by clinicians of internal medicine. If I am obliged to give approximate figures, I should say that the latent period in intestinal cancer amounts to one-half to three years.

B) As far as the initial symptoms are concerned, as already stressed in the preceding remarks, they may take extremely variable forms. By these I understand those symptoms which for the first time call the patient's attention to his affliction, regardless of whether or not he seeks medical attention at once. According to my observations I am able to differentiate two groups.

a) Cases without characteristic disturbances of the intestinal canal; to these belong 58 of the 106 cases observed by me, thus more than half, and are given as follows:

1. Forty-three cases of vague gastrointestinal phenomena, for the most part irregularities of bowel movements, in which either obstipation or an inclination to diarrhea existed or both conditions alternated.

2. In 9 cases a tumor of the abdomen was noticed accidentally, without any disturbances whatever on the part of the intestine;

in addition, in 12 cases a tumor was noticed along with the previously mentioned vague gastrointestinal disturbances.

3. In 6 cases there were local peritonitic phenomena which were obviously caused by the ulcerating tumor proceeding to perforation; 5 of these cases concerned a tumor of the cecum which later presented the picture of perityphilitis with abscess formation; in one case perforation of the bladder occurred without any preceding symptoms, cystitis with pneumaturia being the alarming symptom.

b) Cases in which the symptoms manifested themselves as definite disturbances of the intestinal canal, 48. Of these, 39 cases had signs of chronic intestinal stenosis, 5 with acute ileus without prodromal symptoms; 4 cases could be regarded as chronic ileus, that is, as borderline cases between chronic intestinal stenosis and acute ileus.

C) To regard the period of clinically demonstrable symptoms as a special state of the disease is obviously entirely arbitrary, for the beginning of this stage depends on when the patient seeks medical aid. Many times, as for example in all cases of ileus, this stage coincides with the initial stage. But after all we are permitted to decide on some sort of a classification of this kind, as far as we are definitely able to make the diagnosis at a time when the patient knows himself to be so seriously ill that he seeks aid in earnest, namely from a surgeon. Of the 106 cases seeking our aid, 84 (80 per cent) already showed outspoken functional disturbances on the part of the intestine, and indeed in 45 cases signs of a pronounced chronic ileus were present, 28 had acute ileus (with these are included 2 cases who had colostomies performed outside of the clinic because of ileus), and 11 cases had a chronic ileus.

In only 22 cases (20 per cent) were typical disturbances of intestinal function lacking. In these cases the intestinal tumor caused the following phenomena:

1. In 7 cases the symptoms were limited to a palpable tumor in the abdomen.

2. Eight times signs of perforation were present; one each of perforation into the general abdominal cavity with peritonitis,

perforation into the bladder and perforation into the stomach; in 5 cases a perityphilitic abscess was present.

3. In 7 cases at the time of clinical observation only vague gastrointestinal symptoms presented:

Thus we see that, at the time of clinical observation, with the exception of 7 cases, severe symptoms always presented, pointing to the diagnosis of intestinal tumor or at least a stenosing or ulcerating intestinal process. So in these cases the diagnosis was determined with sufficient certainty to answer the question for the surgeon as to whether or not operative intervention was in order. It would take me too long to go further into the difficulties of the differential diagnosis between intestinal carcinoma and other stenosing and ulcerating processes of the intestine. Frequently enough, the surgeon must be satisfied with the general diagnosis of "Intestinal Tumor" or "Intestinal Stenosis", and if no contraindications are present, the possibility of an intestinal carcinoma justified an exploratory laparotomy, by means of which the further diagnosis and the nature of the operation to be undertaken must then be decided. Thus far a precise differential diagnosis of the primary disease is of but slight practical significance. On the other hand, in one respect in our treatment, we must sharply separate the clinical manifestations of intestinal carcinoma from other more insidious symptoms according to whether the case presents the picture of acute ileus or chronic intestinal stenosis. Many experienced surgeons, even Koerte, have referred to this point; but nevertheless it should not be held as a binding rule to regard a case of intestinal carcinoma with acute ileus and one without ileus as two diseases, which not only are to be regarded with different prognoses but also to be handled differently in regard to operative therapy. The patient showing chronic symptoms of intestinal carcinoma, if he is well nourished and if no extensive metastases, ascites or advanced cachexia are present, has as a rule sufficient resistance to stand severe action, in particular, radical operation. We can avoid the chief danger, that of peritoneal infection, almost with assurity by the two stage method of resection to be described later. On the other hand a carcinomatous patient with

acute ileus is in all ways a much poorer risk. At the most he is no longer equal to a major intraabdominal operation, even if technically favorable for intestinal resection. At this point it would take too long to present all the reasons for this. Statistics show that patients with acute ileus, for the most part, succumb to procedures which patients of the first category withstand easily. Only exceptionally is such a patient successfully brought through a resection. The three cases on which I operated all expired. (One, it is true, had successfully weathered the main operation, the first act of the two stage resection and died only at a further operation.) Enteroanastomosis alone would be too severe a procedure in most cases. Therefore we should limit ourselves to the necessary minimum of action in ileus due to intestinal carcinoma; that is, first of all perform only the colostomy, and if the tumor is suitable for resection, carry this out only at a second session, after the over-congested bowel whose nourishment has been severely damaged, as well as the patient, have completely recovered themselves.

After what has been said no further explanation is needed if, out of my 106 cases, I separate the 23 which were brought to the clinic with acute ileus from the remaining 83. Among the latter are also found those which were previously stricken with acute ileus elsewhere than the clinic and in which, after successful colostomy, we performed a second operation.

We will now consider the latter cases, those with chronic symptoms who came under our care. As you know, along with resection, simple colostomy and intestinal anastomosis, with complete or incomplete exclusion of intestine are at our disposal as palliative measures. We are not always in a position to decide previously as to whether the radical operation will be possible or whether we will be limited to one of the palliative operations. In these cases the operation will have to begin as an exploratory incision. In general we are agreed on the principles which should lead us to the choice between radical operation and one of the palliative procedures as soon as the abdominal cavity is opened. Still, in individual cases, it will depend a great deal on personal experience as to whether the operator decides on the

extensive radical operation or on a palliative operation or indeed if he close the abdominal cavity without having effected his object. Previously, when I used the single stage resection as a rule, I decided on resection only under favorable general and local conditions. Since I have used the incomparable less dangerous two stage method I go much further. Naturally, although we review the indications sufficiently, a not inconsiderable number of cases will remain in which we desist from any operation.

The 83 cases of malignant tumor with chronic symptoms are arranged according to treatment used as follows:

Not operated on.....	17 ¹		
Exploratory incision.....	7	0	
Colostomy.....	6	0	
Intestinal anastomosis with exclusion of bowel.....	16	3	
Resection.....	37	11	29.7%
Of these, single stage with primary suture.....	21	9	42.9%
Two stage with protrusion.....	16	2	12.5%

There is nothing special to be noted in regard to the direct results of simple exploratory incision and the palliative operations. On the other hand, to go further into the results of the radical operation will be well worth while. Without further ado the great superiority of the two stage method of resection over the single stage with primary suture strikes the eye. In the latter a mortality of 42.9 per cent, in the former only 12.5 per cent. The result appears even more favorable when we consider that the two deaths with the two stage method can not be charged to the operation itself. One case died seven weeks after operation from marasmus, a result of carcinoma metastases; in the second case peritonitis was the cause of death and indeed resulted from rupture of the carcinomatous infiltrated descending colon, which was adherent to the transverse colon and tore on being loosened.

As far as I am acquainted with the literature the single stage resection of the carcinomatous gut with primary suture is still

¹ Of these, one case died in the clinic. Operations as a rule were avoided because of too extreme cachexia, metastases, etc. Several times the patient refused the proposed operation.

today almost generally in vogue. Up to now the results of this operation are far from satisfactory, even for carcinoma in the region of the large bowel alone, regardless of whether the union of gut is brought about by the old method of circular intestinal suture or through lateral implantation or apposition or finally with the intestinal button. I need only quote a few statistical counts. Of Koerte's 19 cases of radical operation, 7 died (of these to be sure 3 were operated on with ileus), of Czerny's 18 cases 9 died, of von Bramann's 14 cases 6 died, of Kroenlein's 12 cases 6 died. The extensive statistics of DeBovis, who has collected 104 cases from associated series of well known surgeons, coincide fairly well with these figures. The mortality amounts to 38.4 per cent. In addition DeBovis has collected 51 fatal cases following single stage resection from other individual publications. Thirteen times collapse, 30 times peritonitis was the cause of death. Also interesting is the fact that in cases treated without drainage of the peritoneal cavity, the mortality was one-third higher than that of the drained cases. The cases of death from collapse indicate that the operation was too severe for a considerable portion of the patients. The 30 cases of peritonitis indicate that, in more than half of the fatal cases, either the peritoneum was infected during the operation or peritonitis subsequently developed because of defect of the sutures. Without a doubt the danger of peritoneal infection, whether primary or secondary to defect of the sutures, is enormously great. That is easily understood if we consider the conditions under which the intestinal suture is undertaken. Intestinal union in the large bowel (of this only do we speak here) is in itself not very reliable, whatever method we may employ. The lessened strength of the wall of the large gut, the poorer blood supply, the sluggish peristalsis as a result of which the firm feces stagnate at the site of suture, give far less assurance of primary union than in the small intestine; added to these is the fact that in intestinal carcinoma as a rule they are not normal segments of intestine which we join to one another. The segment above is commonly overdistended and as result is poorly nourished; also it is often paretic which further increases

the stagnation and the insecurity of the sutures. The danger of primary infection of the peritoneum from the opened intestine is regarded as much greater than is commonly accepted. Even if we carefully separate the portion of gut to be resected from the remainder of the peritoneal cavity by temporary tamponade, the spread of intestinal bacteria in the serosa itself throughout a wide range is not prohibited. Hans Buchbinder,¹ in an interesting work, has demonstrated that the bacteria from the finest puncture of the gut spread over the surface of the serosa with great rapidity, and indeed not only on that portion directly concerned but also on the neighboring loops of bowel. Accordingly we must consider that in every gastric and intestinal operation a certain number of bacteria gain admission to the peritoneal cavity in spite of all precautions. The longer the operation lasts, the greater the number of bacteria will be. Now doubtless in many cases, we can almost say as a rule, a slight amount of bacterial invasion is overcome by the peritoneum; the effect produced is the circumscribed peritonitis observed in all stomach and intestinal operations, leading to partially protective adhesions in the region of the suture. The capacity to overcome successfully an insignificant peritoneal infection of such a nature, depends in the first place on the resistance of the entire organism. The patient with acute ileus is, as a result of the intestinal intoxication, so lacking in resistance that he can not overcome a minimum of infection. Also in chronic intestinal stenosis which we know accompanies intestinal cancer as a rule, the patient is found in a state of chronic intoxication, by which he is doubtless less resistant to intestinal bacilli. In this we find sufficient explanation for the poor results of the single stage resection of the intestine for cancer. I do not doubt that the frequent pneumonias following this operation in part at least are to be attributed to a bacterial infection of the peritoneum which locally is overcome but which leads to pneumonia by way of small pulmonary emboli.

¹ Experimental Investigations on Living Animal and Human Intestine, *Deutsche Zeitschrift für Chirurgie*, vol. 55, p. 458.

There is no doubt therefore that we can produce an improvement in the results only if we:

1. Make the operation less severe and so lessen the danger of collapse, and
2. Prevent peritoneal infection during the operation and during the course of healing. By means of the two stage operation we accomplish both.

The idea of removing intestinal carcinoma by a two stage operation is in no way new. Even at the end of the year '70, Schede, Gussenbauer, Maydl, v. Volkmann and others found themselves forced, partly because of the technical impossibility of uniting the intestinal extremities by suture after resection of the tumor, and partly because loss of strength of the patient demanded a rapid termination of the operation,—as I say, they were forced to close the abdomen with the formation of an artificial anus. The latter could be closed if conditions justified it. Along with this two stage operation resulting from necessity, other combinations were later used, namely, formation of an artificial anus above the stenosed area at a time when ileus existed, and resection with typical intestinal suture at a later time. A further commonly known combination is that of primary intestinal anastomosis with partial or complete exclusion of the diseased portion of gut and extirpation of the tumor at a later sitting. The two last named combinations have the great advantage that they, first of all, empty the proximal bowel and thus do away with the secondary changes. The second operation is then carried out on approximately normal intestinal parts. However, these two combinations do not avoid one of the chief sources of danger, namely, the primary and secondary infection of the peritoneum. This danger, along with all others, is best avoided by the two stage operation, which for more than five years now I have performed on practically all tumors of the large bowel. Essentially the operation consists of freeing the tumor of all connections, as in the single stage resection, up to the communication with the afferent and efferent segment of gut. The tumor, thus mobilized, is brought out through the abdominal wound and the latter closed off up to the point of exit of the two

sections of bowel; the tumor is resected extraperitoneally either at once or after the course of twelve to forty-eight hours. The resulting artificial anus is later closed.

The principle of this procedure was, to my knowledge, first employed by Oscar Block in Copenhagen in the year 1892. In a case of ileus he found the cause to be a freely movable tumor situated in the sigmoid flexure. He brought this out on the abdominal wall together with the long meso-sigmoid and incised the gut above the tumor. After the subsidence of symptoms of ileus he carried out an extraperitoneal resection, followed in four months by closure of the artificial anus with circular intestinal suture. Block at first recommended this procedure only for intestinal tumors with movable mesentery and at that time expressed the conviction that the greatest dangers of the operation were avoided by the extra-abdominal resection of the bowel. Two years later he advanced a step further, in that he mobilized a less movable tumor of the descending colon sufficiently by incising the fold of the root of mesentery and peritoneum. Whether Block later went still further and resected the mesentery primarily in the manner which I employ, I do not know. At any rate, the idea is not much different. It is clear that the original procedure of Block, disregarding its limited applicability, has the great disadvantage that the regional lymph glands remain unnoticed because the mesentery is left undisturbed. Other surgeons besides Block have carried out a similar procedure in similar cases; for instance, Allingham, W. Edmunds, Hochenegg, and others. In all I find that DeBovis describes eight operations of this type, all ending with favorable results. I have already mentioned that of my sixteen cases only two terminated fatally and that in both instances this method of operation had no bearing on the fatal outcome. The operation, as it has been worked out in my clinic during the course of recent years, shapes itself in detail in the following way.

The intestinal tumor along with the diseased lymph glands and the corresponding portion of mesentery are freed from all attachments as in the single stage resection, so that the tumor is finally connected only with the gut leading to and from it.

The mesentery must be loosened sufficiently to allow the section of bowel which is to be resected to be laid out on the surface of the abdomen without tension. When this is done the abdominal wall is closed off so that only the cleft necessary for the passage of the afferent and efferent segments of gut is left open; this cleft must not be so narrow that the afferent section is compressed. A series of serosal sutures is placed at the point where parietal peritoneum comes in contact with the protruding portions of bowel, these sutures also closing off the peritoneal cavity at this point. The outer skin is sutured carefully to the protruding bowel (without tamponades). Next the line of suture as well as the surface of contact between exposed gut and skin wound are thickly spread with zinc paste and over this a sterile dressing is placed. Over the bandage comes a large piece of water-proof material with a slit just large enough to allow the protruding gut to be drawn through. Thus the tumor which is to be resected is finally separated from the abdominal cavity not only by the sutured abdominal wall but also by the protective dressing. Formerly I removed the tumor only after the passing of twelve to forty-eight hours, but now I usually do it at once. A thick glass tube is fastened into the discharging segment of gut and a thick rubber tube fastened to the glass one, so that the intestinal contents flow off.

The wound in the abdominal wall in this procedure heals, as far as it is sutured, by primary intention. After two to three weeks, by means of my spur-crusher, I transform the artificial anus resulting from the removal of the tumor first into a fecal fistula and later make a closure by suture.

The advantages of this procedure are evident. The main operation is shorter than by the single stage method, the peritoneal infection during the operation is absolutely avoided, and one can thus attempt it much earlier on a patient debilitated by the disease. A further advantage is that the operation can be performed in cases of wide extension of the tumor or in deep locations, as for example in the lower part of the sigmoid flexure, where it would be too dangerous to unite the intestine because of too forceful tension on the loops of gut. The method is not

only less dangerous but also more easily performed. Of course the procedure also has its drawbacks. The duration of treatment is longer and the patient operated on must bear with the unpleasantness of an artificial anus for a long time. But I think these disadvantages are greatly outweighed by the advantages of greater safety and increased ease of performance.

Accordingly I do not hesitate to recommend the previously described procedure of two stage resection of intestine as the logical method in all cases of tumors of the large bowel, even if no complications are present. In the small intestine, if acute ileus is not present, I use the single stage resection with primary suture. Tumors of the cecum I regard as borderline cases. I depend on the strength of the patient, on the condition of the proximal bowel and on the more or less technical difficulty in freeing the tumor, as to whether or not primary suture will be the suitable closure. If after freeing of the tumor, a broad traumatized surface devoid of peritoneum remains, as is usually the case, so that a larger dead space remains, I perform the two stage operation.

Allow me, Gentlemen, briefly to go into the existing results of my operation. First of all we will consider the end results of radical operation. In this, the method of operation, whether single or two stage, makes no great difference. Therefore I have taken the liberty of grouping together cases operated on by the single stage and two stage. The table presented gives you an explanation of the subsequent fate of 20 patients operated on, of whom we have definite information.

Radical Operation

37 cases, of these 11 died. Surviving: 26 cases. No information obtained of 6. (Two of these discharged with recurrences.)

In all, 20 cases remain. Of these:

1. Died with recurrences, 9 cases as follows:

1 case after $5\frac{1}{2}$ years

1 case after $14\frac{1}{3}$ months

1 case after 13 months

1 case after 11 months

- 1 case after 8 months
- 1 case after 7 months
- 1 case after 6 months
- 1 case after $5\frac{1}{2}$ months
- 1 case after $3\frac{1}{2}$ months

Summary: 9 cases, average length of life post-operative 15 months.

2. Living with recurrence, 1 case after 13 months.
3. Living and free from recurrence, 10 cases as follows:
 - 1 case, $9\frac{1}{4}$ years
 - 1 case, $5\frac{3}{4}$ years
 - 1 case, $4\frac{3}{4}$ years
 - 1 case, $4\frac{1}{4}$ years
 - 1 case, 4 years
 - 1 case, 2 years
 - 1 case, $1\frac{1}{2}$ years
 - 1 case, $1\frac{1}{4}$ years
 - 2 cases, $\frac{1}{4}$ year

Operation was performed more than 4 years ago on 12 cases which survived the operation itself. Of these 5 are to be regarded as radically cured.

As you see, the end result, if we regard a period of four years free from recurrence as permanent cure, is very encouraging. Indeed, it has long been proven that permanent cure lasting for a decade and longer really can occur following resection for intestinal cancer. I need only mention the well known cases of Gussebauer-Martinie, v. Bergmann, Rehn, v. Bramann, Czerny, Kroenlein, Frank, Hochenegg, Lilienthal, and Koerte. Also one case from my early period of observation has remained free from recurrences for sixteen years. But such a single observation gives us no information as to the expectations of radical cure on which we can reckon in individual cases. Perhaps this will be made possible later by more extensive statistical compilations. However, the present experience affords us the most favorable hopes. In Koerte's report I find among the 12 cases in which operation is at least four years ago, 4 which have remained free from recurrence. Taken with my figures this gives 24 cases with 9 permanent cures or 37.5 per cent.

The two following tables give information on the end results of palliative operations in intestinal cancer.

Colostomy

There have lived:

A. Since the onset of the disease:

- 1 case, $6\frac{1}{2}$ years
- 1 case, $4\frac{1}{2}$ years
- 3 cases, $3\frac{3}{4}$ years
- 1 case, $2\frac{3}{4}$ years
- 1 case, $2\frac{1}{2}$ years
- 1 case, $2\frac{1}{4}$ years
- 1 case, 2 years

Average: 3 years, 6 months.

B. Since the operation:

- 1 case, $4\frac{1}{2}$ years
- 1 case, $3\frac{1}{4}$ years
- 1 case, $2\frac{3}{4}$ years
- 2 cases, 2 years
- 1 case, $1\frac{1}{4}$ years
- 1 case, 10 months
- 1 case, 5 months
- 1 case, $2\frac{1}{2}$ years
- 1 case, $1\frac{1}{2}$ years

Average: 1 year, 9 months.

Intestinal Anastomosis

A. Since the onset of disease:

- 1 case, $3\frac{1}{2}$ years
- 1 case, 2 years
- 1 case, $1\frac{1}{2}$ years
- 1 case, $1\frac{1}{4}$ years
- 2 cases, 11 months
- 1 case, 7 months

Average: 1 year, $6\frac{1}{3}$ months.

B. Since the operation:

- 1 case, $9\frac{1}{2}$ months

1 case, 9 months

3 cases, 7 months

1 case, $6\frac{1}{2}$ months

1 case, $4\frac{1}{2}$ months

1 case, $1\frac{1}{2}$ months

Average: $8\frac{1}{2}$ months.

The duration of life of individual cases after colostomy is strikingly long. In these patients we have attempted to determine the length of life from the beginning of the first symptoms of disease and the length after operation, in order to form a picture relating to the duration of patients with intestinal carcinoma as a class.¹ As you see, we find here strikingly higher figures which do not coincide with the view hitherto existing in regard to the duration of life in intestinal carcinoma. This estimation in general has been too low. For the sake of completeness we have sought to acquaint ourselves with the fate of patients not operated on or subjected to an exploratory incision only. The results here, as will be apparent to you from the following table, are much more unfavorable.

Non-operative Cases and Exploratory Incision

There have lived since the appearance of the first symptoms:

1 case, 20 months

1 case, 18 months

1 case, 17 months

1 case, 12 months

2 cases, 9 months

1 case, 8 months

1 case, 3 months

Average: 12 months.

Obviously these were from the beginning more malignant, more quickly growing carcinomas, which, therefore, did not lend themselves to operation.

In regard to the results of operation in ileus resulting from

¹ The total count of cases listed under A is smaller for colostomy as well as enterostomy than under B because in all cases the beginning of the disease could not be definitely determined.

intestinal cancer I can limit myself, since the pertinent observations will be more exhaustively described in a later communication from my clinic on ileus. Of 23 cases which entered the clinic with acute ileus and were operated on, 12 recovered from the ileus; 11 died. The difference in the prognosis according to the location of the obstructing carcinoma is striking, the higher it lies, the more unfavorable the prognosis. Fourteen times the tumor was situated in the sigmoid flexure, and only 3 of those operated on died; while of the 9 patients with high location of the cancer, 8 died. Furthermore, our material, even though limited in amount, shows that the less severe the procedures instituted, the better the prognosis. Of 15 cases in which only an artificial anus was made, only 4 died. On 10 occasions the carcinoma was situated in the sigmoid flexure, and only 1 died following colostomy. The two cases in which enteroanastomosis was done died, as did 5 cases in which resection was performed.

After these practical experiences, it is understandable that I have made it a principle to limit myself to simple colostomy as a rule in cases of ileus due to intestinal cancer. I would undertake the two stage resection only in exceptional cases where conditions are especially favorable. The simple colostomy has, along with others, the enormous advantage that it can be performed under local anesthesia. The procedure is thus almost completely without danger. The performance of colostomy under local anesthesia presupposes that we can localize the site of the obstruction with approximate certainty. With our present day diagnostic aids this is possible in the great majority of cases. If, in spite of these, a mistake is made and if an incision for an "anus sigmoideus" is made without finding the distended loop of bowel, one will do less harm by making a second incision in the ileocecal region under local anesthesia, than by opening the abdominal cavity widely under narcosis and thus seeking for the obstruction.

(THE END)

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Thomas Addison M.D.

From *The Worthies of Cumberland*, by Henry Lonsdale. London, 1873

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Thomas Addison

English Physician, 1793-1860

BIOGRAPHY

- 1793 Born in April at Long Benton, near Newcastle. Educated at Newcastle Grammar School.
- 1815 Age 22. Graduated with doctor's degree in medicine from University of Edinburgh, with thesis in Latin "De Siphilide." Became house surgeon to Lock Hospital, London, and worked with the great dermatologist, Bateman.
- 1820 Age 27. Became associated with Guy's Hospital, probably only as a student.
- 1824 Age 31. Appointed assistant physician at Guy's Hospital.
- 1827 Age 34. Lectured on *Materia Medica* at the same institution.
- 1829 Age 36. Wrote first book in English on action of poisons on the living body.
- 1837 Age 42. Became physician to Guy's Hospital and joint lecturer on medicine with Dr. Richard Bright. First used static electricity in treatment of spasmodic and convulsive diseases.
- 1839 Age 46. Described appendicitis.
- 1849 Age 56. Described pernicious anemia and disease of the suprarenal capsules (melasma suprarenale or Addison's disease), in a paper before the South London Medical Society.
- 1860 Age 67. Died on June 29, at Brighton, shortly after his retirement. Buried in Lauercost Abbey, Cumberland.

Addison's reputation as a clinical teacher contributed perhaps more than any of his colleagues, including Richard Bright, to the fame of Guy's Hospital as a school of medicine. His personality was the exact opposite to Bright's, being blunt, nervous, and even arrogant to conceal his innate shyness.

EPONYMS

1. ANEMIA: Pernicious or Addison-Biermer. *On the Constitutional and Local Effects of Disease of the Supra-renal Capsules*, viii, 43 pp., 11 pl. fol., London, Highley, 1855. Also in *Collected Writings*, New Sydenham Society, London, 1868, p. 212.
2. DISEASE: Chronic suprarenal insufficiency, usually due to tuberculosis of suprarenal capsules. 1st announcement. *Anemia—disease of the suprarenal capsules*. *Lond. Med. Gaz.*, n. s., 43: 517-518, 1849. 1st paper. *On the Constitutional and Local Effects of Disease of the Supra-renal Capsules*, viii, 43 pp., 11 pl. fol., London, Highley, 1855. Also in *Collected Writings*, New Sydenham Society, London, 1868, pp. 209-239.
3. KELOID: Morphea. *On the Keloid of Alibert, and on True Keloid*, 1854. In *Collected Writings*, 1868, pp. 165-185.
4. PILL: Calomel, digitalis and squills for hepatic dropsy in syphilis; called also Guy's or Baillie's pill.

BIBLIOGRAPHY OF WRITINGS

A—Army Medical Library.

B—New York State Library.

C—New York Academy of Medicine Library.

D—John Crerar Library of Chicago.

1. An essay on the operation of poisonous agents upon the living body. With John Morgan. viii, 91 pp., 8°, London, Longman, 1829, in A.
2. Observations on the disorders of females connected with uterine irritation. viii, 96 pp., 8°, London, Highley, 1830, in A & C. Also in: *Collected Writings*, 1868, pp. 109-154.

3. Observations on fatty degeneration of the liver. Guy's Hosp. Rep., 1 s., 1: 476-485, 1836.
 4. Case of ovarian dropsy, removed by the accidental rupture of the cyst. Ibid., 41-42.
 5. On the influence of electricity as a remedy in certain convulsive and spasmodic diseases. Ibid., 2: 493-507, 1837.
 6. Observations on the diagnosis of pneumonia. Ibid., 57-67.
 7. On the disorders of the brain, connected with diseased kidneys. Ibid., 4: 1-7, 1839.
 8. Elements of the practice of medicine. With Richard Bright. 8°, London, 1839, in A, C and D.
 9. Observations on the anatomy of the lungs. (Read before the Royal Med. & Surg. Soc., 1840.) In Collected Writings, 1868, pp. 1-6.
 10. Observations on pneumonia and its consequences. Guy's Hosp. Rep., 2 s., 1: 365-402, 1843.
 11. On the pathology of phthisis. Ibid., 3: 1-38, 1845.
 12. On the difficulties and fallacies attending physical diagnosis in diseases of the chest. Ibid., 4: 1-36, 1846. Also: 36 pp., 8°, London, 1846, in A.
 13. Anemia—disease of the supra-renal capsules. Lond. Med. Gaz., n. s., 43: 517-518, 1849.
 14. On a certain affection of the skin, vitiligoidea—a. plana, b. tuberosa, with remarks. With William Gull. Guy's Hosp. Rep., 2. s., 7: 265-276, 1851.
 15. On the keloid of Alibert, or on true keloid. Med.-Chir. Trans., Lond., 37: 27, 1854. Also in Collected Writings, 1868, pp. 165-185.
 16. On the constitutional and local effects of disease of the supra-renal capsules. viii, 43 pp., 11 pl., fol., London, Highley, 1855, in A and C. Also in Collected Writings, 1868, pp. 209-239.
- (Same) Die Erkrankungen des Nebennieren und ihr Folgen. Zum ersten Male in deutscher Übersetzung herausgegeben und eigeleitet von Erick Ebstein. 47 pp., 1 pl., 8°. Forms No. 20 in Klassiker der Medizin, edited by K. Sudhoff. Leipzig, Barth, 1912.

- (Same) A clinical study of Addison's disease. Mayo Clinic Monographs. By L. G. Rowntree and A. M. Snell. Phila. Saunders, pp. 30-53, 1931.
17. A collection of the published writings of the late Thomas Addison. By Dr. Wilks and Dr. Daldy. 239 pp., 8°, London, New Sydenham Society, 1868, in A, B, C and D.

BIBLIOGRAPHY OF BIOGRAPHIES

- Obituary. Med. Times & Gaz., 2: 20, 1860.
- Biography. The Worthies of Cumberland by Lonsdall, H., London, 4: 239, 1873.
- Obituary. Guy's Hosp. Gaz., 3: 193; 201, 1874.
- Biography. Roll of the Royal College of Physicians, London. 2. ed., 3: 205, 1878.
- Biography by Boase, F. Modern English Biography. London, 1882.
- Biography. Eminent Doctors, Their Lives and Their Works by Bethany, G. T., London, 1885.
- Biography by Payne, J. F. Dict. Nat. Biog. London, 1: 133, 1885.
- Biography. Intercol. Med. Jour. Australas., Melbourne, 10: 212-215, 1905.
- Biography. Guy's Hosp. Gaz., 22: 520-524, 1908.
- Biography by Winne, Jr., C. K. Albany Med. Ann., 29: 664-669, 1908.
- Biography by Ebstein, E. München. med. Wochenschr., 59: 23-38, 1912.
- Biography; contributors to the science of medicine. Med. Jour. & Rec., 120: 339-340, Oct. 1, 1924.
- Biography by Hale-White, W., Guy's Hosp. Rep., 76: 253-279, July, 1926.
- Doctor and patient in Addison's journals. By Bragman, L. J. Med. Jour. & Rec., 125: 483; 558, 1927.
- Thomas Addison and Richard Bright, contemporaries. By Oppenheimer, R. H. Ibid., 126: 20; 107, 1927.
- Biography; Addison's disease. Am. J. Surg., 8: 1312, 1930.
- Biography. Colorado Med., 28: 420; 461, 1931.

Biography. Jour. Organotherapy, 16: 84, 1932.

Addison and his discovery of idiopathic anemia. By Long, E. R.,
Ann. Med. Hist., 7: 130-132, 1935.

Biography by Carbonero, R. Muñoz. Crón. méd., Valencia, 39:
953-954, 1935.

Biography in Great Doctors of the Nineteenth Century. By
Hale-White, Sir W. pp. 106-123, London, Arnold, 1935.

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ADDISON'S ANEMIA

Pernicious or Addison-Biermer anemia is described in a general, clinical way in Addison's first announcement, *Anemia—disease of the supra-renal capsules*, in Lond. Med. Gaz., n. s., 43: 517-518, 1849. The author was attempting to find an explanation for many cases of anemia which he had carefully studied and followed. The description, although brief, clearly gives the clinical picture of anemia but does not mention pigmentation of the skin. In the three patients who were examined after death, disease of the supra-renal capsules was found.

In his paper *On the Constitutional and Local Effects of Disease of the Supra-renal Capsules* (viii, 43 pp., 11 pl., fol., London, Highley, 1855), Addison writes:

"For a long period I had from time to time met with a remarkable form of general anemia, occurring without any discoverable cause whatever—cases in which there had been no previous loss of blood, no exhausting diarrhea, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease.

Accordingly, in speaking of this form in clinical lecture, I perhaps with little propriety applied to it the term 'idiopathic,' to distinguish it from cases in which there existed more or less evidence of some of the usual causes or concomitants of the anemic state."

In the next seven paragraphs are described the characteristics of this "idiopathic" anemia but Addison concludes, "I have failed to discover any organic lesion that could properly or reasonably be assigned as an adequate cause of such serious consequences." The balance of the paper then concerns disease of the supra-renal capsules.

Thus we see that Addison had recognized the importance of this "idiopathic" anemia but was unable to throw much light on it. This great clinician deserves to be remembered because he struggled to clear up the mysteries of the anemias and, reaching the first mile-post, gave impetus to later workers.

Anton Biermer of Zurich in 1872 reported a series of cases of progressive pernicious anemia. (*Form von progressiver pernicioser Anämie*, Cor.-Bl. f. schweiz. Ärzte, Basel, II: 15, 1872.) He was given credit in Germany and France for describing for the first time a new clinical condition. But just as he had been preceded by Addison in 1855, so the latter had been anteceded by Combe in 1823, by Andral in 1823, by Marshall Hall in 1837, Piörny in 1841 and Pearce in 1845. (French, H., in Allbutt and Rolleston, *System of Medicine*, London, Macmillan, 5: 728, 1909.)



Anemia: Disease of the Supra-renal Capsules

Published in *The London Medical Gazette*, n.s: 8: 517-518, 1849

DR. ADDISON, at the request of the President, proceeded to describe a remarkable form of anemia, which, although incidently noticed by various writers, had not attracted, as he thought, by any means the attention it really deserved. It was a state of general anemia incident to adult males, and had for several years past been with him a subject of earnest inquiry and of deep interest. It usually occurs between the ages of twenty and sixty; sometimes proceeding to an extreme degree in a few weeks, but more frequently commencing insidiously, and proceeding very slowly, so as to occupy a period of several weeks, or even months, before any very serious alarm is taken either by the patient or by the patient's friends. Its approach is first indicated by a certain amount of languor and restlessness, to which presently succeed a manifest paleness of the countenance, loss of muscular strength, general relaxation or feebleness of the whole frame, and indisposition to, or incapacity for, bodily or mental exertion. These symptoms go on increasing with greater or less rapidity: the face, lips, conjunctivae, and external surface of the body, become more and more bloodless; the tongue appears pale and flabby; the heart's action gets exceedingly enfeebled, with a weak, soft, usually large, but always strikingly compressible pulse; the appetite may or may not be lost; the patient experiences a distressing and increasing sense of helplessness and faintness; the heart is excited, or rendered tumultuous in its action, the breath-

ing painfully hurried by the slightest exertion, whilst the whole surface bears some resemblance to a bad wax figure; the patient is no longer able to rise from his bed; slight edema perhaps shows itself about the ankles; the feeling of faintness and weakness becomes extreme, and he dies either from sheer exhaustion, or death is preceded by signs of passive effusion or cerebral oppression. With all this, the emaciation or wasting of the body, though sometimes considerable, is not unfrequently quite disproportionate to the failure of the powers of the circulation—relaxation and flabbiness, rather than wasting of the flesh, being one of the most remarkable features of the disorder.

Dr. Addison next proceeded to give the details of several cases which had fallen under his own immediate observation. In only two of these did the patients recover: the one, a man below the middle period of life, who was looked upon as past all hope, and suspected to be suffering from some latent malignant disease, slowly but steadily recovered under the free use of brandy, but with the singular result of the hair of one side of his head turning permanently grey, whilst the other retained its original brown color. The second case of recovery occurred in a gentleman above middle age: it was by no means far advanced, but was sufficiently well marked to excite alarm. He left his business, quitted London, and sought recreation in the country. After a time he returned, and appeared to have shaken off the disorder almost entirely. In three cases only was there an inspection of the body after death, and *in all of them was found a diseased condition of the supra-renal capsules*. In two of the cases no disease whatever could be detected in any other part of the body. Dr. Addison inquired if it were possible for all this to be merely coincidental? It might be so, but he thought not, and making every allowance for the bias and prejudice inseparable from the hope or vanity of an original discovery, he confessed that he felt it very difficult to be persuaded that it was so. On the contrary, he could not help entertaining a very strong impression that these hitherto mysterious bodies—the supra-renal capsules—may be either directly or indirectly concerned in sanguification; and that a diseased condition of them, functional or structural, may inter-

fere with the proper elaboration of the body generally, or of the red particles more especially. At all events, he considered that the time had arrived when he felt himself warranted in directing the attention of the profession to these curious facts. In thanking the Society for the patient hearing with which they had favored him, he ventured to bespeak their interest not only in regard to the anemia he had described, but also in cases of purpura, and some of the more anemiated forms of chlorosis in the female, which he could not but regard as being more or less allied to the morbid state to which he had directed their attention. Indeed, not only had he found the anemia in question occasionally occurring in connection with purpura, but had observed in cases of the latter disorder certain local symptoms which pointed somewhat significantly to the seat of the suprarenal capsules; whilst the bloodless and waxy appearance of certain chlorotic females bore so close a resemblance to the anemia described, that it was difficult not to suspect the existence of something common to both.

THE END

ADDISON'S DISEASE

For many years Thomas Addison had studied the mysteries of the anemias and had collected a series of cases of peculiar pigmentation of the skin with languor and debility. After 29 years of association with Guy's Hospital and its "Great Men", he made his first announcement (see the attending pages) before the South London Medical Society on pathologic changes in the suprarenal capsules. Six years later, in 1855, Addison published a book of 43 pages and 11 plates, *On the Constitutional and Local Effects of Disease of the Supra-renal Capsules*. This is reproduced here in its entirety. He then recognized that disease of these organs was always accompanied by changes in the pigmentation of the skin, "a dark, dingy or smoky-looking discoloration". He gives several case histories with their complete necropsy findings. Although the changes in the suprarenal gland are usually due to tuberculosis, rarely there may be malignant metastases or unexplained atrophy; Addison's 11 case reports include some of these rare conditions. We are not here concerned with his attempt to associate such changes with the etiology of anemia but we must appreciate Addison's keen clinical observations and subsequent post-mortem examinations. He was a pioneer in the study of suprarenal gland pathology.

It was Armand Trousseau (1801-1867) who first proposed to call the suprarenal syndrome, "Addison's disease". After reviewing the records of many cases, O. Brenner (Quart. Jour. Med., 22: 121, 1928) concluded that the symptoms of Addison's disease occur only when most of the cortex is destroyed and even if the suprarenal medulla and the chromaffin tissues are normal.

Recent progress in the treatment of Addison's disease has concerned the use of epinephrin to tolerance, the Muirhead regimen, as reported by Dr. A. L. Muirhead, Professor of Pharmacology at Creighton University College of Medicine, Omaha, in *An auto-graph history of a case of Addison's disease*. (Jour. Amer. Med. Assn., 76: 652-653, 1921.) Dr. Muirhead was treated in the Mayo Clinic by Dr. L. G. Rowntree who, after Dr. Muirhead's death, reported *Subsequent course of a case of Addison's disease*. (Ibid., 79: 556-557, 1922.)

Renewed hope in therapy arose from the discovery by Swingle and Piffner (Science, 71: 321-322, 1930) that an extract of the

suprarenal cortex would maintain indefinitely the life of completely suprarenalectomized cats. This material was used on patients in the Mayo Clinic by Rowntree and his associates and reported "strikingly effective in these cases and life saving in some". (Jour. Amer. Med. Assn., 96: 231; 97: 1446, 1931.)

Additional work has been done by J. M. Rogoff of Western Reserve University School of Medicine, Cleveland, with "an extract representing the active substance or hormone (inter-renalin) of the adrenal cortex". (Ibid., 92: 1569-1571; 99: 1309-1315, 1932.) "The outlook for relief—has been rendered more encouraging through the tentative indications, in the experiments of Stewart, Rogoff and others, that replacement therapy may become a reality". (Editorial, Ibid., 93: 1734, 1929.)

A test for the presence of Addison's disease was suggested by G. A. Harrop and his co-workers. (Ibid., 100: 1850-1855, 1933.) Signs of early relapse of Addison's disease are produced by a restriction of sodium chloride. These signs usually appear between the third and fifth day of the test. In the blood sodium and chloride are lowered, potassium and nitrogen are increased and there is a diminution in the blood volume. After the signs are established prompt recovery follows intravenous administration of a physiologic solution of sodium chloride. E. M. Kline has recently demonstrated the value of this test. (Ibid., 108: 1592-1593, 1937.)

Addison's paper of 1855 is reproduced here by the kind permission of the New York Academy of Medicine.

The plates in the original publication are approximately 8 by 12 inches in size and are colored in the manner of 1855. In comparison to the standard of today, the color of the plates is unnatural and exaggerated. They are therefore reproduced here without color.



On the Constitutional and Local Effects of Disease of the Supra-renal Capsules

BY

THOMAS ADDISON, M.D.

Senior Physician to Guy's Hospital

Published by Samuel Highley, London, 1855

To The Right Honourable Lord Hawke, as a tribute of respect, and in grateful acknowledgment of a long, cordial, and most disinterested friendship, this little work is dedicated by His Lordship's obliged friend and humble servant,
THOMAS ADDISON.

PREFACE

IF PATHOLOGY be to disease what Physiology is to health, it appears reasonable to conclude, that in any given structure or organ, the laws of the former will be as fixed and significant as those of the latter; and that the peculiar characters of any structure or organ may be as certainly recognized in the phenomena of disease as in the phenomena of health. When investigating the pathology of the lungs, I was led, by the results of inflammation affecting the lung-tissue, to infer, contrary to general belief, that the lining of the air-cells was not identical and continuous with that of the bronchi; and microscopic investigation has since demonstrated in a very striking manner the correctness of that inference,—an inference, be it

observed, drawn entirely from the indications furnished by pathology. Although Pathology therefore, as a branch of medical science, is necessarily founded on Physiology, questions may nevertheless arise regarding the true character of a structure or organ, to which occasionally the pathologist may be able to return a more satisfactory and decisive reply than the physiologist,—these two branches of medical knowledge being thus found mutually to advance and illustrate each other. Indeed, as regards the functions of individual organs, the mutual aids of these two branches of knowledge are probably much more nearly balanced than many may be disposed to admit; for in estimating them, we are very apt to forget how large an amount of our present physiological knowledge, respecting the functions of these organs, has been the immediate result of casual observations made on the effects of disease. Most of the important organs of the body, however, are so amenable to direct observation and experiment, that in respect to them the modern physiologist may fairly lay claim to a large preponderance of importance, not only in establishing the solid foundation, but in raising and greatly strengthening the superstructure of a rational pathology. There are still, however, certain organs of the body, the actual functions and influence of which have hitherto entirely eluded the researches and bid defiance to the united efforts of both physiologist and pathologist. Of these not the least remarkable are the “Supra-Renal Capsules,”—the *Atrabiliary* Capsules of Caspar Bartholinus; and it is as a first and feeble step towards an inquiry into the functions and influence of these organs, suggested by Pathology, that I now put forth the following pages.

T. A.

24 New Street, Spring Gardens,
May 21, 1855.

It will hardly be disputed that at the present moment, the functions of the supra-renal capsules, and the influence they exercise in the general economy, are almost or altogether unknown. The large supply of blood which they receive from three

separate sources; their numerous nerves, derived immediately from the semilunar ganglia and solar plexus; their early development in the foetus; their unimpaired integrity to the latest period of life; and their peculiar gland-like structure; all point to the performance of some important office: nevertheless, beyond an ill-defined impression, founded on a consideration of their ultimate organization, that, in common with the spleen, thymus and thyroid body, they in some way or other minister to the elaboration of the blood, I am not aware that any modern authority has ventured to assign to them any special function or influence whatever.

To the physiologist and to the scientific anatomist, therefore, they continue to be objects of deep interest, and doubtless both the physiologist and anatomist will be inclined to welcome, and regard with indulgence, the smallest contribution calculated to open out any new source of inquiry (p. 2) respecting them. But if the obscurity, which at present so entirely conceals from us the uses of these organs, justify the feeblest attempt to add to our scanty stock of knowledge, it is not less true, on the other hand, that any one presuming to make such an attempt, ought to take care that he do not, by hasty pretensions, or by partial and prejudiced observation, or by an over-statement of facts, incur the just rebuke of those possessing a sounder and more dispassionate judgement than himself. Under the influence of these considerations I have for a considerable period withheld, and now venture to publish, the few facts bearing upon the subject that have fallen within my own knowledge; believing as I now do, that these concurring facts, in relation to each other, are not merely casual coincidences, but are such as admit of a fair and logical inference—an inference, that where these concurrent facts are observed, we may pronounce with considerable confidence, the existence of diseased supra-renal capsules.

As a preface to my subject, it may not be altogether without interest or unprofitable, to give a brief narrative of the circumstances and observations by which I have been led to my present convictions.

For a long period I had from time to time met with a very remarkable form of general anæmia, occurring without any dis-

coverable cause whatever; cases in which there had been no previous loss of blood, no exhausting diarrhœa, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease. Accordingly, in speaking of this form of anæmia in clinical lecture, I, perhaps with little propriety, applied to it the term "idiopathic," to distinguish it from cases in which there existed more or less evidence of some of the usual causes or concomitants of the anæmic state.

The disease presented in every instance the same general character, pursued a similar course, and, with scarcely a single exception, was followed, after a variable period, by the same fatal result. It occurs in both sexes, generally, but not exclusively, beyond the middle period of life, and so far as I at present know, chiefly in persons of a somewhat (p. 3) large and bulky frame, and with a strongly-marked tendency to the formation of fat. It makes its approach in so slow and insidious a manner, that the patient can hardly fix a date to his earliest feeling of that languor, which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement; there is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth and waxy appearance; the lips, gums and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitations being produced by the most trifling exertion or emotion; some slight œdema is probably perceived about the ankles; the debility becomes extreme, the patient can no longer rise from his bed, the mind occasionally wanders, he falls into a prostrate and half-torpid state, and at length expires: nevertheless to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the amount of obesity often present a most striking contrast to the failure and exhaustion observable in every other respect.

With, perhaps, a single exception, the disease, in my own ex-

perience, resisted all remedial efforts, and sooner or later terminated fatally. On examining the bodies of such patients after death, I have failed to discover any organic lesion that could properly or reasonably be assigned as an adequate cause of such serious consequences; nevertheless, from the disease having uniformly occurred in fat people, I was naturally led to entertain a suspicion that some form of fatty degeneration might have a share at least in its production; and I may observe, that in the case last examined, the heart had undergone such a change, and that a portion of the semilunar ganglion and solar plexus, on being subjected to microscopic examination, was pronounced by Mr. Quekett to have passed into a (p. 4) corresponding condition. Whether any, or all, of these morbid changes are essentially concerned, as I believe they are, in giving rise to this very remarkable disease, future observation will probably decide.

The cases having occurred prior to the publication of Dr. Bennett's interesting essay on "Leucocythæmia," it was not determined by microscopic examination whether there did, or did not, exist an excess of white corpuscles in the blood of such patients.

It was whilst seeking in vain to throw some additional light upon this form of anæmia, that I stumbled upon the curious facts, which it is my more immediate object now to make known to the Profession; and however unimportant or unsatisfactory they may at first sight appear, I cannot but indulge the hope, that by attracting the attention and enlisting the coöperation of the Profession at large, they may lead to the subject being properly examined and sifted, and the inquiry so extended, as to suggest, at least, some interesting physiological speculations, if not still more important practical indications.

The leading and characteristic features of the morbid state to which I would direct attention, are, anæmia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin, occurring in connexion with a diseased condition of the "suprarenal capsules."

As has been observed in other forms of anæmic disease, this

singular disorder usually commences in such a manner, that the individual has considerable difficulty in assigning the number of weeks or even months that have elapsed since he first experienced indications of failing health and strength; the rapidity, however, with which the morbid change takes place, varies in different instances. In some cases that rapidity is very great, a few weeks proving sufficient to break up the powers of the constitution, or even to destroy life; the result, I believe, being determined by the extent, and by the more or less speedy development, of the organic lesion. The patient, in most of the cases I have seen, has been observed gradually to fall off in general health; he becomes languid (p. 5) and weak, indisposed to either bodily or mental exertion; the appetite is impaired or entirely lost; the whites of the eyes become pearly; the pulse small and feeble, or perhaps somewhat large, but excessively soft and compressible; the body wastes, without, however, presenting the dry and shrivelled skin, and extreme emaciation, usually attendant on protracted malignant disease; slight pain or uneasiness is from time to time referred to the region of the stomach, and there is occasionally actual vomiting, which in one instance was both urgent and distressing; and it is by no means uncommon for the patient to manifest indications of disturbed cerebral circulation. Notwithstanding these unequivocal signs of feeble circulation, anæmia, and general prostration, neither the most diligent inquiry, nor the most careful physical examination, tends to throw the slightest gleam of light upon the precise nature of the patient's malady: nor do we succeed in fixing upon any special lesion as the cause of this gradual and extraordinary constitutional change. We may indeed suspect some malignant or strumous disease; we may be led to inquire into the condition of the so-called blood-making organs; but we discover no proof of organic change anywhere,—no enlargement of spleen, thyroid, thymus or lymphatic glands,—no evidence of renal disease, of purpura, of previous exhausting diarrhœa, or ague, or any long-continued exposure to miasmatic influences: but with a more or less manifestation of the symptoms already enumerated, we discover a most remarkable, and, so far as I know, characteristic discoloration taking place in the skin,—

sufficiently marked indeed as generally to have attracted the attention of the patient himself, or of the patient's friends. This discoloration pervades the whole surface of the body, but is commonly most strongly manifested on the face, neck, superior extremities, penis and scrotum, and in the flexures of the axillæ and around the navel. It may be said to present a dingy or smoky appearance, or various tints or shades of deep amber or chestnut-brown; and in one instance the skin was so universally and so deeply darkened, that, but for the features, the patient might have been mistaken for a mulatto.

(p. 6) In some cases this discoloration occurs in patches, or perhaps rather certain parts are so much darker than others, as to impart to the surface a mottled or somewhat checkered appearance; and in one instance there were, in the midst of this dark mottling, certain insular portions of the integument presenting a blanched or morbidly white appearance, either in consequence of these portions having remained altogether unaffected by the disease, and thereby contrasting strongly with the surrounding skin, or, as I believe, from an actual defect of colouring matter in these parts. Indeed, as will appear in the subsequent cases, this irregular distribution of pigment-cells is by no means limited to the integument, but is occasionally also made manifest on some of the internal structures. We have seen it in the form of small black spots, beneath the peritoneum of the mesentery and omentum—a form which in one instance presented itself on the skin of the abdomen.

This singular discoloration usually increases with the advance of the disease; the anæmia, languor, failure of appetite, and feebleness of the heart, become aggravated; a darkish streak usually appears upon the commissure of the lips; the body wastes, but without the extreme emaciation and dry harsh condition of the surface so commonly observed in ordinary malignant diseases; the pulse becomes smaller and weaker, and without any special complaint of pain or uneasiness, the patient at length gradually sinks and expires. In one case, which may be said to have been acute in its development as well as rapid in its course, and in which both capsules were found universally diseased after death,

the mottled or checkered discoloration was very manifest, the anæmic condition strongly marked, and the sickness and vomiting urgent; but the pulse, instead of being small and feeble as usual, was large, soft, extremely compressible, and jerking on the slightest exertion or emotion, and the patient speedily died.

My experience, though necessarily limited, leads to a belief that the disease is by no means of very rare occurrence, and that were we better acquainted with its symptoms and progress, we should probably succeed (p. 7) in detecting many cases, which, in the present state of our knowledge, may be entirely overlooked or misunderstood; and, I think, I may with some confidence affirm, that although partial disease of the capsules may give rise to symptoms, and to a condition of the general system, extremely equivocal and inconclusive, yet that a more extensive lesion will be found to produce a state, which may not only create a suspicion, but be pronounced with some confidence to arise from the lesion in question. When the lesion is acute and rapid, I believe the anæmia, prostration, and peculiar condition of the skin will present a corresponding character, and that whether acute or chronic, provided the lesion involve the entire structure of both organs, death will inevitably be the consequence.

If this statement be correct, and I quite believe it to be so, the chief difficulty that remains to be surmounted by further experience in this, I fear, irremediable disease, is a correct and certain diagnosis;—how we may at the earliest possible period detect the existence of this form of anæmia, and how it is to be distinguished from other forms of anæmic disorder. As I have already observed, the great distinctive mark of this form of anæmia is the singular dingy or dark discoloration of the skin; nevertheless at a very early period of the disorder, and when the capsules are less extensively diseased, the discoloration may, doubtless, be so slight and equivocal as to render the source of the anæmic condition uncertain. Our doubts, in such cases, will have reference chiefly to the sallow anæmic conditions resulting from miasmatic poisoning or malignant visceral disease; but a searching inquiry into the history of the case, and a careful examination of the several parts or organs usually involved in anæmic disease, will

furnish a considerable amount of at least negative evidence; and when we fail to discover any of the other well-known sources of that condition, when the attendant symptoms resemble those numerated as accompanying disease of the capsules, and when to all this is superadded a dark, dingy or smoky-looking discoloration of the integument, we shall be justified at least in entertaining a strong suspicion in some instances,—a suspicion almost amounting to certainty in others. It must, however, (p. 8) be observed, that every tinge of yellow, or mere sallowness, throws a still greater doubt over the true nature of the case, and that the more decidedly the discoloration partakes of the character described, the stronger ought to be our impression as to the capsular origin of the disorder.

The morbid appearances discovered after death will be described with the cases in which they occurred; but I may remark that a recent dissection (March 1855) has shown that even malignant disease may exist in both capsules, without giving rise to any marked discoloration of the skin; but, in the case alluded to, the deposit in each capsule was exceedingly minute, and could not have seriously interfered with the functions of the organs: extensive and fatal malignant disease had, however, affected other parts. It may be observed in conclusion, that on subjecting the blood of a patient, who recently died from a well-marked attack of this singular disease, to microscopic examination, a considerable excess of white corpuscles was found to be present.

p. 9 CASE I.*—REPORTED BY MR. THOMAS FULLER

James Wootten, æt. 32, admitted into Guy's Hospital, under Dr. Golding Bird, Feb. 6, 1850, has been residing at Long Alley, Moorfields, and is by occupation a baker. States that he was attacked with a cough three years since, which he was unable to get rid of by ordinary remedies, and was finally cured at St. Bartholomew's, after taking pills for one week. From this time, his skin, previously white, began to assume a darker hue, which has been gradually increasing. Twelve months after leaving the

*The cases generally are given in the language and style of their respective reporters.

above hospital he was laid up from excessive weakness, the result of his cough, which had again appeared, and incapacitated him for his work. He now became an out-patient of St. Thomas's, under Dr. Goolden, who cured his cough, and thinking that the colour of his skin depended on jaundice, treated him for that disease, but to no purpose. He left the hospital in tolerable health, but subsequently lost flesh, and became so excessively weak, the colour of his skin at the same time getting rapidly darker, that he applied for admission here, which was granted him.

Present Appearances.—The whole of the skin on the body is now of a dark hue, and he has just the appearance of having descended from coloured parents, which he assures me is not the case, nor have any of his family for generations, that he can answer for, manifested this peculiarity. The colour of the skin does not at all resemble that produced by the absorption of the nitrate of silver, but has more the appearance of the pigment of the choroid of the eye; it seems to have affected some parts of his body more than others, the scrotum and penis being the darkest, the soles of the feet and palms of the hands the lightest; the cheeks are a little sunken, the nose is pointed, the conjunctivæ are of a pearly (p. 10) whiteness; the voice is puny and puerile, the patient speaking with a kind of indescribable whine, and his whole demeanour is childish. He complains of a sense of soreness in the chest about the scrobiculus cordis. The chest is well-formed and perfectly resonant; the sounds of the heart are also healthy; there is some slight fullness in the region of the stomach. The urine is of a proper colour, and he has passed in twelve hours one and a half pint, which has a specific gravity 1008, an acid reaction, and contains neither albumen nor sugar; there is also some pain on pressure in the left lumbar region.

Feb. 8.—Dr. Bird wished a likeness to be taken, so as to be able to watch any alterations in his colour; and considering the case one of anæmia, ordered Syr. Ferri Iodidi ʒj ter die; and middle diet. These he took the whole of the time that he was in the hospital, and was discharged in April, rather stronger, but the colour remaining precisely the same.

Shortly after his discharge from the hospital, he was seized with acute pericarditis and pulmonic inflammation, under which he speedily sank and died.

The following is a report of the post-mortem examination:—

Lungs universally adherent, the adhesions being very old. The upper lobe of the right lung contained some small defined patches of recent pneumonia, about the size of a crown-piece, surrounded by tolerably healthy structure. The lower lobe was extremely fleshy and without air. The left lung was bound down by old pleuritic adhesions, which were very tough and difficult to be torn through. The substance of this lung was fleshy, and contained but little air. There was no tubercle or cavity. The mucous membrane of the bronchial tubes was considerably injected, and, I believe, rather thickened. The pericardium was distended with fluid of a deep brown colour, amounting to about half-a-pint; recent lymph was effused over the whole serous surface. The liver and spleen were (p. 11) both of weak texture, and easily broken down; the structure of the liver rather coarse. The gall-ducts pervious. The gall-bladder contained the usual quantity of bile, which was thin, watery and clear. The thoracic duct was pervious throughout; and there was no obstruction to any of the veins or arteries that I could discover. The colour of the blood in the arteries had an unusually dark appearance. The kidneys were quite healthy and of full size. The supra-renal capsules were diseased on both sides, the left about the size of a hen's egg, with the head of the pancreas firmly tied down to it by adhesions. Both capsules were as hard as stones. Intestines pale. Lumbar glands natural. No tubercular deposit was discovered in any organ. The head was not examined. (Vide Pl. I.)

In some of the cases about to be given, the capsules merely participated in disease affecting other organs, either of a strumous or malignant character, and it might consequently be doubtful whether the peculiar symptoms depended upon such complications, or upon the special disease of the capsules.

In the above instance, however, no such doubt could reasonably

be entertained, inasmuch as there was found no abnormal condition whatever of any other organ, to which these peculiar symptoms could by any means be attributed. The slow and gradual inroads of the disease, and the remarkable excess of pigment, were sufficiently accounted for by the universality of the change that had taken place in the structure of both capsules; at least such would be the legitimate conclusion to be drawn from a comparison of the present with other cases about to be related.

(p. 12)

CASE II

James Jackson, æt. 35. The subject of this case was admitted into the Clinical ward, under my own care, November 11, 1851, and died December 7, 1851. For the particulars of its history and result, I am indebted to my former pupil and present distinguished colleague, Dr. Gull, who was the first to suspect the true nature of the malady during the life of the patient.

A married man, residing at Gravesend, and occupied as a tide-waiter in the Customs. Of a bilious temperament, dark hair and sallow complexion, which since his illness has much deepened, so that now it is of a dark olive-brown. His wife says, "This obvious change in his complexion has been from the beginning of his illness, and gradually came on at that time."

There can be no doubt as to this change in the complexion depending upon increase of pigment, for if the lips be turned down, the mucous membrane is seen to be mottled by a deposit of pigment, and a closer examination shows that the dark colour of the lips, which at first had the appearance of sordes, is dependent upon the presence of a black pigment, which is not movable by moistening or washing the lips. There is an expression of anxiety in the face, and the brow is contracted. He gives the following history of himself:—

His occupation subjects him to much anxiety; he is exposed to all the vicissitudes of the weather, both night and day, and sometimes his food for weeks together consists of salt provisions. Eight years ago he had rheumatism, accompanied with great nervous depression; since that time he has enjoyed general good

health, with the exception of some attacks of (p. 13) bilious vomiting. His present illness came on six months ago with headache, vomiting and constipation. About the sixth day of his illness he became delirious, and was insensible for twenty-four hours. On recovering his consciousness, he was unable to move the fingers of either hand, nor could he move the legs below the knees; the same parts were numb, as was also the tip of the tongue. He continued weak during the whole summer.

Two months ago he resumed his occupation, and remained at it until ten days back, when the old symptoms of headache, vomiting and constipation returned. Dr. McWilliam saw him at this time, and found his symptoms to have an intermittent character, and regarded the case as one of miasmatic poisoning, not only from his general symptoms, but also from the dark poisoned look of his face, not altogether unlike that presented on the approach of the asphyxic stage of cholera.

On his admission into the hospital, the pulse was extremely small and feeble, the expression of the face pinched, the brows knitted. He vomited mucus containing altered blood of a dark brown colour; tongue clean; epigastric region full, especially towards the left side, where he has had some twitching pain and slight tenderness on pressure. Urine natural in colour and quantity, of a light brown colour, not coagulable by heat. He went on, day by day, with but slight symptoms of change. Skin cool; pulse moderate in frequency, but extremely feeble, so as scarcely to be felt at the wrist. On several occasions the depression was so great as to require the exhibition of decided stimulants. There was a continued tendency to sickness. The abdomen soft, with marked aortic pulsation. Bowels constipated; chest everywhere resonant; heart's sounds normal; extent of dullness on percussion not increased. Slight traces of intermittence in the symptoms; the surface in the evening being cool, or even cold, and the following morning warm, as if from reaction.

Probable diagnosis.—The epigastric tenderness and pulsation, with frequent vomiting, and the ejected mucus and altered blood, point to an inflammatory condition of the gastric mucous membrane. But what (p. 14) condition of system is it which favours

the production of black pigment? Is it some affection of the liver; or is it, as Dr. Addison supposes, disease of the supra-renal capsules?

Sectio Cadaveris

The lining membrane of the stomach was finely injected into minute puncta and stellæ of a bright red colour, with two or three spots of ecchymosis. The structure of the membrane was thickened and pulpy, and the surface covered with tenacious mucus. In some parts there were irregular superficial abrasions; these appearances of the mucous membrane becoming very distinct by examining it under water by aid of sunlight, and seeming, moreover, unequivocally to demonstrate the existence of a gastritis. The brain, lungs, heart, spleen, liver and kidneys were normal.

The supra-renal capsules contained both of them compact fibrinous concretions, seated in the structure of the organ; superficially examined they were not unlike some forms of strumous tubercle. (Vide Pl. II. and Pl. VIII. figs. 4, 5.)

The slow and insidious approach and progress of the constitutional loss of strength, the extreme feebleness of the pulse, the absence of all evidence of any lesion sufficient to account for the patient's declining condition, the loss of appetite, the uneasiness and irritability of the stomach, and the indications of disturbed cerebral circulation, were all so strongly marked, and so exactly corresponded in kind with what have been observed to accompany the most extensive disease of the capsules, that, coupled with the excess of dark pigment in the integument, we did not hesitate to anticipate with much confidence an extensively diseased condition of these organs.

P. 15

CASE III.—REPORTED BY MR. WILLIAMS

Henry Patten, æt. 26, a carpenter and window-blind maker, residing at 13 Brandon Street, Walworth, was admitted Nov. 9, 1854, having been for some time an out-patient under Dr. Rees.

His habits have been somewhat intemperate; his drink chiefly

malt liquor and spirits. With the exception of a sister, who died of phthisis, all his relations are healthy. He has been married four years. The patient states that up to six months ago, he enjoyed very good health, but then began to be troubled with what he calls "rheumatic" pains in the right leg, which, without laying him up, gradually extended to his hips and side, and thence to the bottom of the spine. His back latterly has been very tender, a jerk or jarring movement giving him great pain at that part. He has noticed his lips to have become dark-coloured for the last three months, and more lately his face to be similarly discoloured in patches. For the last month he has discontinued work on account of attacks of giddiness and dimness of sight, accompanied by a peculiar pain at the back of the head and partial loss of consciousness. These attacks would occur several times in the course of the day, upon any unusual exertion, always whilst in the standing posture, and were instantly relieved by sitting or lying down. Since he has discontinued his employment, they have only occurred on getting out of bed in the morning.

It is for the pains and tenderness at the back, and occasional attacks, as above described, with general debility, that he has been attending this hospital as an out-patient.

Present condition.—The patient presents a highly strumous appearance, being thin, pale, and the hair dark and dry. Over the face and forehead, which are of a general yellowish hue, are several patches of darkened (p. 16) skin, and similar black patches on the lips. There is angular curvature at the second, and great tenderness on pressure over the upper three lumbar vertebræ; he complains also of pain at this part upon moving in bed. There is no paralysis, but considerable general debility. His bowels are regular, and the tongue clean, but the appetite is impaired; the urine is clear, moderate in quantity, and not albuminous. Heartsounds normal, but the impulse feeble. Pulse 80, small and weak.

Nov. 10th. ℞ Quinæ Disulph. gr. iss.

Aquæ distill. ℥j.

Syr. Rhœados ℥ss.

Acid. Sulph. dil. m. v.

Ft. Haustus ter die s.—Vin. Alb. ℥iv.

With these medicines and middle diet he continued with no appreciable change until the 24th, when he had a kind of fainting fit upon rising to have his bed made, contrary to an order that he should keep in the recumbent posture. This day his diet was changed to milk, at his own request. He has been once or twice sick after taking his food.

28th.—The sickness has continued, and he today has a troublesome hiccough, for which he was ordered

Jul. Ammon. p. r. n.

29th.—He has had little sleep, the hiccough, unrelieved by the Julep. Ammon., annoying him much. Dr. Barlow, who now took the ward, ordered him

Æther. Chlor. m. v.

Vini Opii m. v.

ex Mist. Camph. t. d. s.

30th.—He is today about the same. Has been sick this morning, the vomited matter consisting of food and drink. The hiccough occasionally ceasing.

Dec. 1st.—Hiccough still very harassing.

R Vini Opii m. x.

Tinct. Castorei m. x.

ex Julep. Pimentæ p. r. n.

(p. 17) This was found to relieve the hiccough somewhat.

2nd.—He seems considerably weaker, and upon approaching him, his eyelids, half-closed, allowed the lower sclerotic of the raised eyeballs to be seen. The tongue was moist and clean, and pulse 80, very weak. On speaking to him he roused up and appeared quite as usual, but soon relapsed into the torpid state again. His blood under the $\frac{1}{4}$ -inch object-glass presented from forty to sixty white corpuscles in each field, mostly scattered about, but some in patches of two or three and six or eight together.

3rd.—Slept better, although the hiccough did not cease. He complains of a constricting pain about the waist; he is tender on pressure over the spleen, where no tumour is to be felt. The tongue today is dry, and beginning to be sordid, teeth dirty, pulse weak. He presents the same typhoid appearances.

4th.—Pulse weaker, dicrotic, 96; roused from the torpid state

with more difficulty than yesterday. He talks very sensibly, but his wife, who watches by his bedside, states that he wanders in the night.

Jul. Ammon. c. Tinct. Castorei m. v. p. r. n.

The blood presented the same appearances under the microscope as before.

5th.—Hiccough continues, is more feeble, pulse scarcely perceptible, lies in a torpid and typhoid state. When roused, said he was sore all over the body. Tongue and teeth sordid.

6th.—Died quietly at 5 A.M.

Sectio Cadaveris

Nine and a half hours after death in cold wet weather. Rigor mortis, but no decomposition. There was not much emaciation, and the axillæ were slightly discoloured. The countenance was paler than in life, but presented the same olive hue, with the dark patches on the face, forehead and lips. There was a psoas abscess on the right side, extending from Poupart's ligament to the diseased vertebræ, and holding about a pint of flaky pus. (p. 18.)

The disease was between the first and second vertebræ, commencing in the cartilage, and nearly destroying the neighbouring vertebræ at their centres. The bone surrounding the cavity was red, soft, and infiltrated with strumous matter.

Pleura and bronchi healthy.

Both lungs contained hard masses of grey strumous pneumonic deposit, mostly in the apices, but also in the lower lobes; these masses presented the appearance of a conglomeration of tubercles, held together by inflammatory matter. Heart and pericardium healthy. Heart's weight $7\frac{1}{2}$ oz. The blood on microscopic examination contained the same excess of white corpuscles observed in life. Stomach healthy, slightly adherent to the left supra-renal capsule; its structure was not affected. Spleen large, firm, $7\frac{1}{2}$ oz. in weight. Corpuscles visible. The pancreas and all other abdominal organs were healthy. The head was not examined.

Each supra-renal capsule was completely destroyed and converted into a mass of strumous disease, the latter of all degrees of

consistency. The left supra-renal capsule had formed at the upper part a close connexion with the outer coat of the stomach. The upper part of this capsule seemed fluid, and of the colour of pus; the lower firmer, and of the consistency of putty. The right capsule had all degrees of consistency from the bottom to the top; the lower part almost fluid and resembling pus, the centre putty-like, and above this the matter could be detached in flakes; and at the top it was quite earthy, separate angular pieces being easily detached. Vide Plates III. and IV.

Although this patient was known to be labouring under a serious affection of the spine, the ordinary indications of disease of the suprarenal capsules were sufficiently prominent to justify the prediction, which was so satisfactorily confirmed by the post-mortem examination. It is also worthy of remark, that although the patient, as usual, suffered considerably from irritability of stomach, there was but little change observable in that organ after death.

p. 19 CASE IV.—REPORTED BY THE WARD CLERK

John Iveson, æt. 22, admitted into Guy's Hospital, March 20, 1854, and died the following day. A stonemason, residing at Lambeth. Last winter he had pain in the stomach and vomiting. He slightly improved, but the day after Christmas was confined to his bed with great pain and vomiting; the vomited matter consisting of a watery fluid. At that time he had "tic douloureux." On admission his extremities were cold, he was almost pulseless, his hands were blue; he had not had any diarrhœa; he had slight pain, or rather soreness in the hypogastric region; he was quite sensible; the pupils were much dilated. He rallied a little after his admission; had no purging, but vomited bilious matter; had no diabetes or albumenuria. He appeared to die from syncope.

Sectio Cadaveris

Seventeen hours after death, weather cold, limbs rigid, body tolerably nourished, face of a dingy colour, also the axillæ and hands. Abdomen not distended.

Head.—The dura mater and sinuses were found to be healthy, the membranes injected and the veins full. There was slight subarachnoid effusion. The grey matter of the cerebrum was rather deep in colour. The brain was in other respects normal.

Chest.—Trachea granular and congested. The right pleura adherent at the posterior and lower parts; on the left side there were firm adhesions at the apex. The bronchi granular; the left apex was a little puckered, and presented several lobules, with iron-grey consolidation and calcareous deposit. The right lung was healthy, with the exception of a single (p. 20) iron-grey consolidation at the apex. The bronchial and mediastinal glands were healthy.

Heart.—Pericardium healthy. There was a white patch on the right ventricle. The right side of the heart was moderately distended with clot, the left entirely and firmly contracted. The valves were healthy, and the muscular fibre, though flaccid, appeared healthy. No fat was found about the heart. Weight 7 oz.

Abdomen.—Peritoneum healthy, viscera moderately contracted. Stomach not distended; at the cardiac extremity there was post-mortem solution of the mucous membrane: towards the lesser curvature it was granular, in some parts destroyed, ulcerated; quite superficially there was arborescent injection. On microscopical examination, mucous and granule-cells were observed. Brunner's glands were very prominent. Ileum with much mucous congestion. Peyer's and solitary glands very distinct, but only hypertrophied. The mesenteric glands were enlarged, firm and white, full of nuclei, hypertrophied.

Large intestines were healthy.

Liver was of normal form and condition; there was a small amount of fat in the cells; weight 2 lbs. 14 oz., containing no arsenic. Gall-bladder healthy; ducts free, but not enlarged. Spleen enlarged, weight 6 oz. Pancreas was healthy.

The two supra-renal capsules together weighed 49 grains; they appeared exceedingly small and atrophied; the right one was natural, firm; the left deformed by contraction; each adherent to surrounding parts by dense areolar tissue. The section gave a

pale and homogeneous aspect; it presented a fibrous tissue, fat and cells about the size of white blood-corpuscles. The lumbar glands were enlarged. The kidneys coarse, weighing 10 oz. The bladder and prostate were healthy. Vide Plate V.

The history of this man's case renders it probable that his disease commenced several months prior to his admission into the hospital, and it is not a little remarkable that his earliest complaint was of sickness, (p. 21) vomiting and pain in the region of the stomach; symptoms which have constituted a more or less prominent feature in every case that has fallen under my notice, and which in the present instance were so urgent as to suggest a suspicion of some acrid poison having been received into the stomach.

How far these gastric symptoms when present are referrible to sympathy existing between the diseased capsules and the stomach—how far they depend upon disturbed circulation within the head—how far they are attributable to accidental or essential gastric inflammation—and how far the inflammatory aspect of the gastric mucous membrane is the mere result of severe and repeated vomiting, a more extended observation will probably determine hereafter. It was from the presence of these gastric symptoms, the extreme and peculiar prostration of the patient's strength, the great feebleness and smallness of the pulse, the anæmiated eye, the absence of any discoverable lesion to account for the patient's condition, and more especially the dingy discoloration of the face, that led before death to a belief that we should on post-mortem examination find disease of the supra-renal capsules.

It is, moreover, of some significance and importance to observe, that in the present instance, the diseased condition of the supra-renal capsules did not result as usual from a deposit either of a strumous or malignant character, but appears rather to have been occasioned by an actual inflammation,—that inflammation having destroyed the integrity of the organs, and finally led to their contraction and atrophy.

p. 22

CASE V

The following, taken from Dr. Bright's Reports of medical cases, presents, according to my belief, a very good illustration of the disease under consideration, and is headed:

"Serous effusion under the arachnoid and into the ventricles in a case of emaciation, with bilious vomiting and diseased renal capsules."

"*Ann Roots* was admitted in July 1829, under one of the surgeons, into Guy's Hospital, on account of a tumour in the left breast and a swelling of the right parotid; but as it was perceived that she was greatly emaciated and apparently sinking, and therefore quite unfit to undergo any operation, she was transferred to the care of the physician.

"*Her complexion was very dark*, her whole person emaciated; she had no cough, and neither tension nor tenderness of abdomen; she had great difficulty in opening her jaw, owing to the glandular swelling, and could not protrude her tongue. There was no indication but to support the strength. Her stomach soon became irritable; she had bilious vomiting, which reduced her strength, and for a day or two before her death, which took place on the 18th of August, she became drowsy, yet capable of being roused; complaining of some pain over the forehead, and occasionally wandering a little in her intellects.

"In the absence of all positive symptoms, I concluded that it was possible some glandular disease, similar to that which had shown itself below the mammæ and under the jaw, might exist internally, giving rise to emaciation and vomiting; and it appeared probable that serous effusion had been going on in the head for the last few days.

p. 23

"Sectio Cadaveris"

"Considerable emaciation; and on removing the integuments the scalpel opened into an abscess, containing an ounce or two of pus, situated beneath the mamma of the left side. The dura mater was firmly attached to the skull at the vertex, where the bone was remarkably thin, and indented by the glandulæ Pac-

chioni, and the ordinary opaque deposit which surrounds them; on raising the dura mater several small opacities were observable on the arachnoid, and a very considerable quantity of serous fluid was effused under the arachnoid, raising it into bladders, as well as filling up the hollow between the convolutions.

"The whole brain was soft and watery, and many vessels showed themselves where horizontal sections were made. In the ventricles about half an ounce of fluid was collected. The choroid plexus was quite exsanguine.

"Slight adhesions of the pleura pulmonalis and pleura costalis were found, but not sufficient to prevent the lungs from collapsing pretty completely when the air was admitted into the chest. The upper lobe of each lung was in an unhealthy state, looking puckered and containing one or two masses of earthy matter, besides several small incipient tubercles; the greater part of the lungs, however, was in a very healthy condition. Heart small, but healthy. In the abdomen slight old adhesions had taken place in various parts, but they were composed of the finest transparent cellular tissue; even the omentum, which was glued by them to various parts both of the intestines and the parietes, had lost none of its natural delicacy and transparency. The intestines were healthy, but stained with bile; the mucous membrane healthy; the liver healthy, and the gall-bladder full of bile; the pancreas healthy, and the spleen also, but just between the pancreas and the spleen a few absorbent glands were enlarged. The glands of the mesentery were also slightly enlarged. The only marked disease was in the renal capsules, both of which were enlarged, lobulated, and the seat of morbid deposits apparently of a scrofulous character; they were at least four times their natural thickness, (p. 24) feeling solid and hard; on the left side one part had gone into suppuration, containing two drachms of yellow pus. The kidneys themselves healthy. The uterus held down by adhesions in the pelvis."

It does not appear that Dr. Bright either entertained a suspicion of the disease of the capsules before death, or was led at any period to associate the colour of the skin with the diseased

condition of these organs, although his well-known sagacity induced him to suggest the probable existence of some internal malignant disease. In this, as in most other cases, we have the same remarkable prostration; the usual gastric symptoms; the same absence of any very obvious and adequate cause of the patient's actual condition, together with a discoloration of the skin, sufficiently striking to have arrested Dr. Bright's attention even during the life of the patient.

p. 25

CASE VI

R. H., Esq., was a member of the bar, somewhere about middle age. I had the satisfaction of attending him in consultation with Dr. Watson and Mr. Barker, when I was informed that he had been getting thin and emaciated during a period of about twelve months. His appearance and symptoms were very remarkable. He was certainly thin, but not strikingly emaciated, and the surface was soft, loose and supple. He was greatly anæmiated; his eyes were pearly; he complained of extreme languor and faintness; his pulse, contrary to what is usual in capsular disease, was of good size, but exquisitely soft and compressible; the impulse of the heart was feeble, and palpitation or throbbing with scrobicular pulsation was immediately produced by the slightest exertion; without pain, the stomach was exceedingly irritable, and vomiting was both urgent and distressing.

With these symptoms, the surface generally presented a dark dingy aspect, and there were observed, chiefly on the face, neck and arms, patches of a rather deep chestnut-brown colour; these chestnut-brown patches were of various sizes and shapes, and were associated here and there with others presenting a singularly white or blanched appearance, arising either in consequence of the latter portions of the integument having remained unaffected, and so contrasting with the surrounding discoloration, or, what is more probable, from their having received a less supply of pigment than natural. A patient inquiry and most careful examination failed to elicit any information, or to detect any lesion, sufficient to afford even a plausible explanation of the patient's singular condition. The violent vomiting pointed to organic,

perhaps carcinomatous disease of the stomach: nevertheless the general condition and (p. 26) symptoms did not in other respects seem to warrant such a conclusion; and coupling the existing condition and symptoms with the irregular deposition of dark pigment in the skin, a suspicion was entertained that the whole might arise from disease of the supra-renal capsules. To the last, however, considerable doubt prevailed amongst us as to the true nature of the case,—chiefly in consequence of the severity and persistence of the vomiting, and from the vomited mucous matters having been occasionally tinged with blood. The patient speedily sank, and the following report of the morbid appearances discovered after death was furnished, I believe, by my distinguished friend Dr. Hodgkin,

“The morbid specimens consisted of part of the stomach and duodenum,—the termination of the small, and the commencement of the large intestines, with the appendix vermiformis, and the renal capsules with a small portion of the kidney. They were taken from a man rather beyond middle life, who for a considerable time had suffered from obstinate derangement of the stomach.

“The coats of the stomach taken unitedly did not produce any preternatural thickness, but rather the reverse; yet there might be a little thickening or increased development of the mucous membrane. The peculiarity of its appearance consisted in a spotted character not very easily described. Near the pylorus it seemed to consist of a very slight degree of that irregularity which Louis has described as the *état mamelonné*, and which appears to be nothing more than the increased development of a natural structure; but in this instance the elevations were smaller in size, and consequently more numerous, though less prominent than those generally seen towards the middle of the stomach, where this appearance is most frequently noticed.

“Further from the pylorus, in the direction of the smaller curvature, smaller spots were seen more scattered and distant from each other, and apparently consisting of opaque lighter-coloured matter, within the semi-transparent substance of the

mucous membrane itself, which was generally (p. 27) of a faint dusky reddish colour. It could not be decided whether these spots depended on any glandular apparatus, yet the idea suggested itself that they might be connected with the follicles of Lieberkühn. Immersion under water, with the intention of facilitating the examination with the microscope, rendered these spots less conspicuous. The largest might equal a small pin's head; the smaller ones scarcely a quarter so large. The duodenum appeared healthy. The portion of small and large intestine, of which the next specimen consisted, offered nothing remarkable in texture. The mucous membrane was tinged with the dingy olive-green of the fæcal contents, and the ileo-colic valve was rather more prominent than usual in the cæcum. The appendix vermiformis was about three inches in length, but much distended, being about an inch in diameter at its commencement, and becoming gradually less towards the free extremity, where it but little exceeded the normal size. Its peritoneal coat was quite healthy; its general thickness was very little increased; its mucous membrane apparently healthy, of greyish colour, from a little black pigment towards the upper part. Its follicular apparatus was nearly or quite imperceptible. It was completely cut off from the interior of the intestine, the mucous membrane forming a cul-de-sac at both extremities, although there was no apparent want of continuity on the exterior; the septum between the two cavities being merely composed of the two mucous membranes united by cellular tissue. No appearance of cicatrix was discovered, indicating that the separation was of long standing, if not congenital. The contents of the appendix consisted principally of a transparent colloid or thick mucoid secretion, partly of a light straw colour, partly tinged with blood. Interspersed through it, but especially towards the upper part, was an opaque white substance of the same consistence, resembling coagulated milk or ground white lead. A few points were blackened by pigments. Examined with the microscope, the transparent portion exhibited no determinate structure, but a slight tendency to filamentous arrangement. The whole portion was made up of a congeries of oil-globules, varying in size, but all

very minute. The (p. 28) black pigment appeared to pervade some of the oil-globules, rather than itself to compose distinct corpuscles. The basis of this collection was undoubtedly the mucus of the appendix itself, retained by the want of any excretory passage.

"The small fragment of kidney appeared to be of healthy structure, but both the renal capsules were enlarged, (the united weight of the two being one and a half ounce,) of rather irregular surface and considerably indurated. When cut into, instead of exhibiting the ordinary appearance of combination of dark and yellow substances, they seemed to consist of a firm, slightly transparent reddish basis, interspersed with irregular spots of opaque yellow matter, the whole bearing a strong resemblance to an enlarged mesenteric gland, mottled with tubercular deposit. Such was probably the nature of the change which the organ had undergone. The naked eye could discover no trace of cystiform arrangement, and the opaque matter when examined with the microscope exhibited a copious amount of fatty matter, but no nucleated cells."

It was to me a matter of much regret that I had not an opportunity of employing an artist to make an exact representation of the singular discoloration observed upon the skin, and the more so, because, although agreeing in general character with those observed in other cases, there was a manifest peculiarity, as well in the intensity, as in the mode of distribution of these discolorations. With universal dinginess of the surface, there were, especially about the neck, hands and arms, several well-defined patches of a deeper, or somewhat chestnut-brown hue, interspersed here and there with blanched or almost dead-white portions of integument, contrasting in a very remarkable manner with both the general dinginess and deeper brown patches; and what is very remarkable, wherever the integument presented the blanched or dead-white appearance, the hairs upon its surface were observed to have turned completely white.

The superiority of a coloured drawing over the most elaborate verbal (p. 29) description, in conveying a correct idea of any

morbid appearance, is so universally felt and acknowledged, that I have great satisfaction in being now able to furnish one, which may most fairly and faithfully be applied to the above case.

Very recently—March 1855—I was requested to visit a patient (Mr. S.) about 60 years of age, who presented, in a strongly marked degree, the indications of diseased renal capsules. The history, mode of attack, the progress, the anæmia, the extreme feebleness of the heart's action, the uneasiness and irritability of the stomach, and the discoloration of the skin, were all such as characterize the disease generally, and bore the closest resemblance to the above case in particular. My belief was that the capsules were affected with malignant disease, and that probably some other structures about the posterior mediastinum might have been in a similar condition, as the patient had slight œdema of both the upper extremities, whilst the lower limbs remained free. Anxious as I was to procure a post-mortem examination, it was most firmly and peremptorily refused, and it was only through the kind and persevering efforts of my friend, Mr. Parrott of Clapham, that I succeeded in gaining permission to have a sketch taken of the discoloured integument. Of course this representation does not carry along with it such authority and conviction as one taken from a subject actually proved to have had diseased capsules. Nevertheless I entertain no doubt whatever that the capsules were diseased; and even if they were not, I hold myself answerable for the most perfect resemblance between the two cases, so far as the affection of the integument was concerned. Vide Pl. XI.

The following case, having been under the care of one of the surgeons for "carcinoma" of the mamma, I have not been able to furnish any record of the symptoms during life. The corpse, however, presented appearances sufficiently striking to arrest the attention, and call forth the correct prediction of Dr. Lloyd the inspector, who kindly furnished me with the following report.

"Sectio Cadaveris

"*M. T.*, æt. 60. Cancerous disease of the mamma, with cancerous degeneration of the supra-renal capsules.

"Sixteen hours after death. Body extremely emaciated; the left mamma presented a very extensive ulcerated phagedænic malignant tumour, occupying the whole of the upper part of the left side of the chest, infiltrating the cellular tissue, the skin and intercostal muscles with carcinomatous material. *The colour of the skin covering the face, arms and chest was of a peculiar light brown swarthy hue.*

"*Chest.*—On raising the sternum and cartilages, it was found that the malignant growth had passed through the pleura and invaded the lung on the left side, for a space of the size of the palm of the hand, by direct continuity of structure. The pleural cavity of the side contained about 16 oz. of dark-coloured fluid. The lower lobe of the left lung was compressed, and sank in water. The upper lobe was healthy. The right lung was healthy.

"*Heart*—was small and flabby.

"*Abdomen.*—The liver was contracted, irregular on its surface, of yellow (p. 31) colour, containing abundance of fat, burning brilliantly in the spirit-lamp; upon its surface were several nodules of cancerous development. The gall-bladder was occupied in its entire extent by a calculus, and did not contain any bile.

"Both supra-renal capsules contained a considerable amount of cancerous deposit, invading their entire structure, and almost obliterating their cavities.

"The kidneys were contracted and granular. The uterus healthy, but atrophied."

I have already expressed my belief that the urgency of the symptoms, and the quick or slow progress of the disease, are determined by the activity or rapidity of the morbid change going on in the capsules, and by the actual amount or degree of that change; and that universal disease of both capsules will in all probability be found to prove uniformly fatal. These views appear to be countenanced by the character, progress and termination of the cases already given, and receive additional con-

firmation from the history of the following, in which the morbid change was limited to a single capsule, and in which the constitutional and local consequences indicated a corresponding result.

p. 32 CASE VIII.—REPORTED BY THE WARD CLERK

Elizabeth Hannah Lawrence, æt. 53, admitted into Guy's Hospital under Dr. Babington, March 30, 1853.

Appearance.—A short woman; emaciated and feeble; skin harsh and dry, and of a darkish hue. The folds of the axillæ were remarkably dark: coloured patches, the size of the palm of the hand, were observed, raised in wrinkles, and resembling a slight Ichthyosis. Also a very dark brown areola around the umbilicus. Hair grey; much long hair on lips and chin.

Previous History.—Is a single woman, has always been a servant, and has been living of late in Trinity Street, Borough. Was always thin, but yet always enjoyed good health.

Present History.—Four months ago an eruption appeared on her body, for the cure of which she went to the Cutaneous Infirmary at Blackfriars. In a short time she was cured, and just as the eruption disappeared, the present stomach symptoms began. For three months she has had vomiting, with pain in the abdomen and back, particularly in the latter. She has thrown up no blood. She was sent to the hospital as a case of malignant disease of the stomach. The stomach can be felt as a hard tumour in the abdomen: no remains of eruption on the skin. The vomiting continued after admission, and in three days she died from exhaustion.

Sectio Cadaveris

External Appearance.—The body that of a small emaciated woman, with a fair skin and dark hair, presenting certain peculiar discolorations. On (p. 33) either side of the neck there was a tawny appearance, which would not have been remarked, had it not been for three still more marked tawny patches, one on the centre of the sternum, the other two under either axilla. The skin also, besides presenting this yellowish-brown appearance, was somewhat raised and wrinkled or corrugated. These marks

led me to prognosticate disease of the supra-renal capsules before opening the body, believing them to be the marks pointed out by Dr. Addison.

Thorax.—The lungs were congested, exuding a frothy serum, and easily lacerable.

Heart.—Small and lacerable. The mediastinal glands in one or two instances carcinomatous.

Abdomen.—Was shrunk and contracted.

Stomach.—The walls of the stomach from the pylorus through the lesser curvature were thickened, presenting on the surface externally a peculiar network appearance, containing a transparent stroma; beneath this, another layer, with its fibres longitudinally arranged, of strong cellular material; within this, the mucous membrane whole and intact; the entire thickness being about three-quarters of an inch at the pylorus, gradually decreasing to a quarter at the commencement of the cardia. The mucous membrane lower down was here and there destroyed by ulceration, and this ulceration in one instance of an eighth of an inch in size. The stomach was contracted and empty; externally to the stomach several of the glands were affected, even to the head of the pancreas, but the pancreas itself was not affected. Several of the lumbar glands were enlarged.

The left supra-renal capsule was infiltrated with malignant material, and closely adherent to the vessels of the kidney. The kidney itself was healthy. The uterus contained three fibrous tumours, the size of walnuts. Vide Pl. VIII. fig. 1, and Pls. IX. and X.

Although this woman only survived four days after her admission into (p. 34) the hospital, we were led by the partial discoloration of the skin to anticipate disease of the capsules, one only of which, however, was found to be implicated. It will have been perceived, that in a certain number of the cases already given, either strumous or malignant disease existed in other parts or organs, as well as in the capsules; and of course, in the midst of such complications, there is often more or less difficulty in satisfactorily unravelling the case in all its details during

life; nevertheless as we know, that without any such complication whatever, mere disease of the capsules themselves has proved sufficient to produce such alarming symptoms and such serious consequences, it cannot with any show of reason be alleged that these peculiar symptoms, when present, arise exclusively from the accidental complication of other organs.

In the present instance, as in some others, the immediate cause of death, as well as of many of the most distressing symptoms during life, was unquestionably carcinomatous disease of the stomach.

p. 35

CASE IX

Thomas Clouston, æt. 58, admitted into Guy's Hospital, February 11, 1852, under Dr. Barlow. A muscular and strong-built man, of a sanguine temperament and dark complexion. He has been a married man, but his wife died about twenty years ago. His occupation has been that of a sailor, and according to his own statement, he has led a very sober life. His general health has been very good. About five years since, he had a hernia in the left inguinal region, for which he has since worn a truss. This has never given him any difficulty to return. About two months ago he came from Liverpool, in which place he had settled, not intending to go to sea again; and was taken on board the *Dreadnought* for stricture. His general health was quite good at this time, but while in the *Dreadnought* he began to lose his appetite and to feel generally unwell; he had likewise some affection of the left eye, in which he is now nearly blind.

On Saturday the 8th he left the ship at his own request, thinking that he might be better on land; after waiting two or three days, he found that he got no better, and his friends advised him to come to the hospital.

Present Symptoms.—He complains of a sensation of sickness, without actual vomiting; and tightness over the epigastrium. His countenance is anxious. He has no pain in any part. He has rigors, followed by mild sweats, every five or six hours, the rigors usually lasting about an hour. The abdomen is tense and tympanitic; not tender to the touch, excepting over the upper

part. The liver does not appear enlarged. His chest is broad and well-formed; the motion of the ribs moderate, resonant on percussion; and the lungs are apparently sound. The heart's sounds are normal. Pulse rather feeble, 80. Tongue injected at the tip and edges, coated with a light brown fur, very dry. Urine of about average (p. 36) quantity, rather large than otherwise; of a high colour, acid, and does not coagulate by heat. The bowels have been regular. After he had been in a few hours, he brought up a large quantity of beer. Ordered

Mist. Efferves. 4tis horis.

Feb. 12.—The sickness has not returned, but he is without any appetite. He slept but little.

Feb. 13.—He is much the same, but has a more sallow and sunken expression of countenance. He complains of nothing but loss of appetite and general debility. His tongue continues dry and coated with a brownish fur. His bowels have been relaxed, and he passed his motions partly involuntarily.

Feb. 14.—No special change.

Feb. 17.—He seems rather better; he had a little breakfast, and enjoyed it.

Feb. 18.—He has relapsed into his former state, having no appetite and complaining of great debility and thirst. He has \mathfrak{z} iv of sherry daily.

Feb. 20.—There is but little change in him, *his countenance appears to grow darker*, and his strength seems gradually failing. His bowels are rather irritable. Ordered

Enema Amyli c. Syr. Papav. \mathfrak{z} ss.

Inf. Cuspariæ \mathfrak{z} iss t. d.

Feb. 25.—He has been getting gradually weaker, without showing any special symptoms in addition to those mentioned. He died this morning.

Sectio Cadaveris

None was allowed beyond the brain and abdomen; of the former there was considerable softening, and a large amount of subarachnoid fluid. The kidneys were slightly enlarged, mottled,

and in some parts the cortical substance was entirely degenerated into fat. A few tubercles were observed on the surface. The tunic was very easily taken from the surface. Tubercles were also observed on the spleen, and on the (p. 37) peritoneum covering the termination of the Ileum. Tubercular deposit was likewise found in one of the supra-renal capsules. Vide Pls. VI. VII.

The development of tubercles on various parts, as well as in one of the supra-renal capsules, sufficiently attests the strumous character of the patient's disease; and it is difficult to divest oneself of the notion that the disease in the supra-renal capsule had some share in producing the peculiar symptoms which immediately preceded the fatal result, whatever importance may be attached to the state of the kidneys and cerebral complication. At all events, the discoloration of the skin indicated before death the existence of capsular disease; and it is worthy of remark, that in this instance the deposition of pigment-cells was not limited to the integument, but was found scattered in small masses over the omentum, the mesentery, and the cellular tissue on the interior of the abdominal parietes.

p. 38

CASE X

Jane Roff, æt. 28. This person was admitted into the Obstetric Ward, labouring under cancer of the uterus, Feb. 4, 1852. She died Feb. 8, and on the 9th the body was placed on the table for inspection. When proceeding to perform this duty, Dr. Lloyd was struck with the peculiar dingy appearance of the skin, and in consequence, prior to commencing, sought me to look at it. The appearance, though not very strongly marked, was certainly such as to create a strong suspicion that something was wrong with the capsules. On exposing the organ on the right side, it presented a perfectly healthy appearance, and we felt disposed to conclude that our anticipation would turn out to be erroneous. On proceeding to examine the left capsule, however, we were much surprised to find a very extraordinary, and, I suspect, an extremely rare condition of parts. A malignant tubercle had

been developed at that precise point, where the large vein escapes from the organ; this tubercle projected into the interior of the vein, so as almost or entirely to obstruct it, and had moreover led to rupture and effusion into, or a sort of apoplexy of the capsule itself.

This case would render it probable that the excess of dark pigment, so characteristic of renal capsular disease, depended rather upon an interruption to some special function, than upon the nature of the organic change; for, with the exception of the manifestly recent sanguineous effusion into its tissue, the capsule itself did not appear to have undergone any considerable deterioration. Vide Pl. VIII. figs. 2, 3.

p. 39

CASE XI

I may observe in conclusion, that very recently there was examined at Guy's Hospital the body of a person—*William Godfrey*—who had died of cancer, affecting the thoracic parietes, and extending through to the lungs. Quite unexpectedly there was found extensive disease of one of the supra-renal capsules; the organ being very much enlarged, and converted into a hard mass of apparently carcinomatous disease. On referring to the notes of the case as taken by the clinical clerk, I found it stated that "*the patient's face presented a dingy hue,*" although he was naturally of a fair complexion, with reddish or sandy hair on the pubes; and, moreover, the face of the corpse was ascertained to present a freckled and dingy appearance, with a slight brown discoloration at the root of the nose and at each angle of the lips. Vide Pl. VIII. figs. 6, 7, 8.

EXPLANATION OF THE PLATES

PLATE I

Head of James Wooten. Both capsules diseased. Case I.

PLATE II

Head of James Jackson. Both capsules diseased. Case II.

PLATE III

Head of James Patten. Both capsules diseased. Case III.

PLATE IV

Fig. 1. The liver of Henry Patten, with the diseased supra-renal capsules *in situ*.

Figs. 2 & 3. Sections of the diseased supra-renal capsules.

PLATE V

Head and part of the trunk of John Iveson. Both capsules diseased. Case IV.

PLATE VI

Head of Thomas Clouston. A single capsule diseased. Case IX.

PLATE VII

Separate parts from Thomas Clouston.

Fig. 1. Portion of small intestine and mesentery with deposits of dark pigment.

Fig. 2. Ditto.

Fig. 3. Portion of omentum with deposits of dark pigment.

Fig. 4. Deposit of dark pigment in the adipose tissue on the inner surface of the internal oblique muscle.

Figs. 5 & 6. Microscopic views of the dark pigment taken from fig. 1, ($\frac{1}{4}$ inch).

Fig. 7. Natural size of the deposit represented in fig. 6.

PLATE VIII

Fig. 1. The left kidney and diseased supra-renal capsule of Elizabeth Lawrence. Case VIII.

Fig. 2. The left supra-renal capsule of Jane Roff, exhibiting a fungoid growth obstructing the vein of the capsule at its entrance into the renal vein. Case X.

Fig. 3. Section of the same, exhibiting sanguineous infiltration of the organ.

Fig. 4. Section of one of the supra-renal capsules of James Jackson, with strumous deposit. Case II.

Fig. 5. Exterior view of the same.

Fig. 6. Kidney and diseased supra-renal capsule of William Godfrey. Case XI.

Fig. 7. Microscopic view displaying meshes composed of a delicate stroma of transparent and fibrous tissue, containing cancer cells, taken from the diseased supra-renal capsule of William Godfrey.

Fig. 8. Cancer juice, consisting of well formed cells, with large nuclei and nucleoli, from the same.

PLATE IX

Neck and part of the trunk of Elizabeth Lawrence. A single capsule diseased. Case VIII.

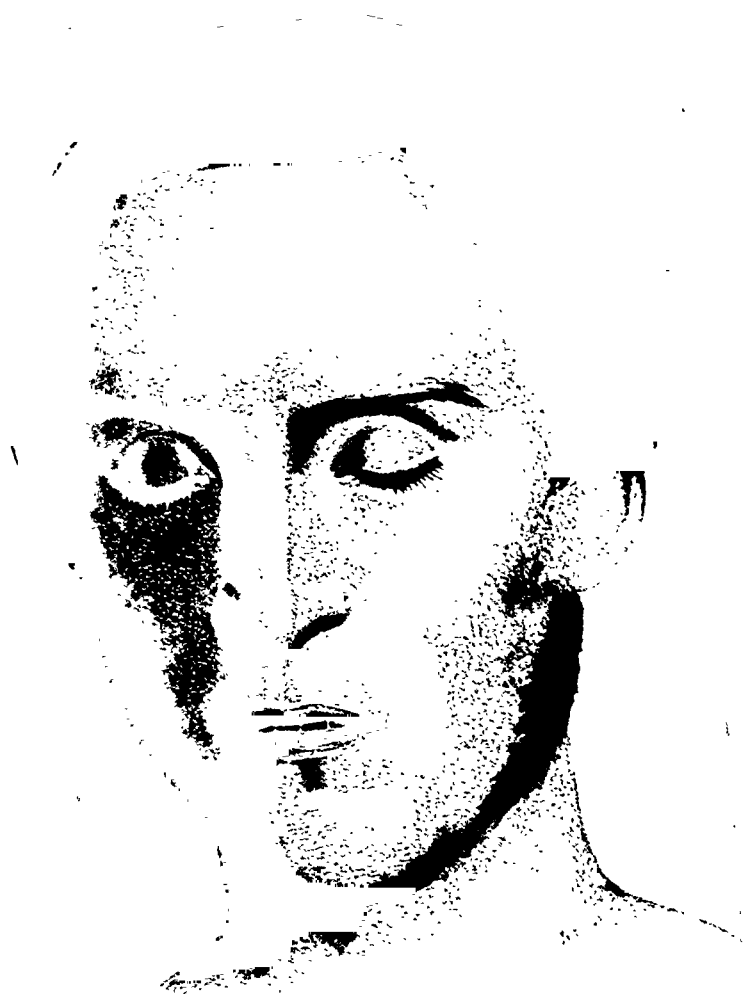
PLATE X

Abdomen of the same, exhibiting general dinginess of the integument, with several small circumscribed deposits of darker pigment.

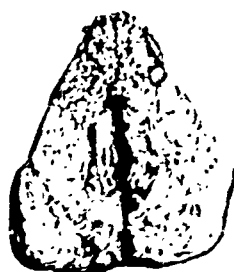
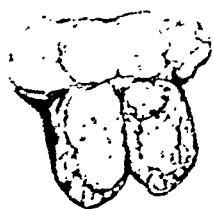
PLATE XI

Head, neck and trunk of Mr. S., exhibiting peculiar discolorations and white patches of the integument, similar to those observed in Case VI.









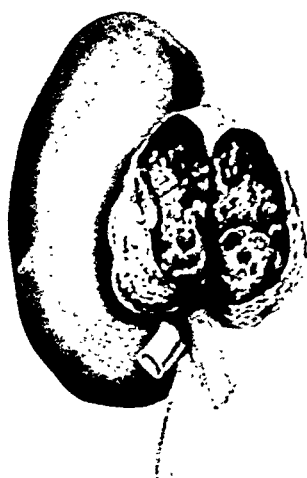


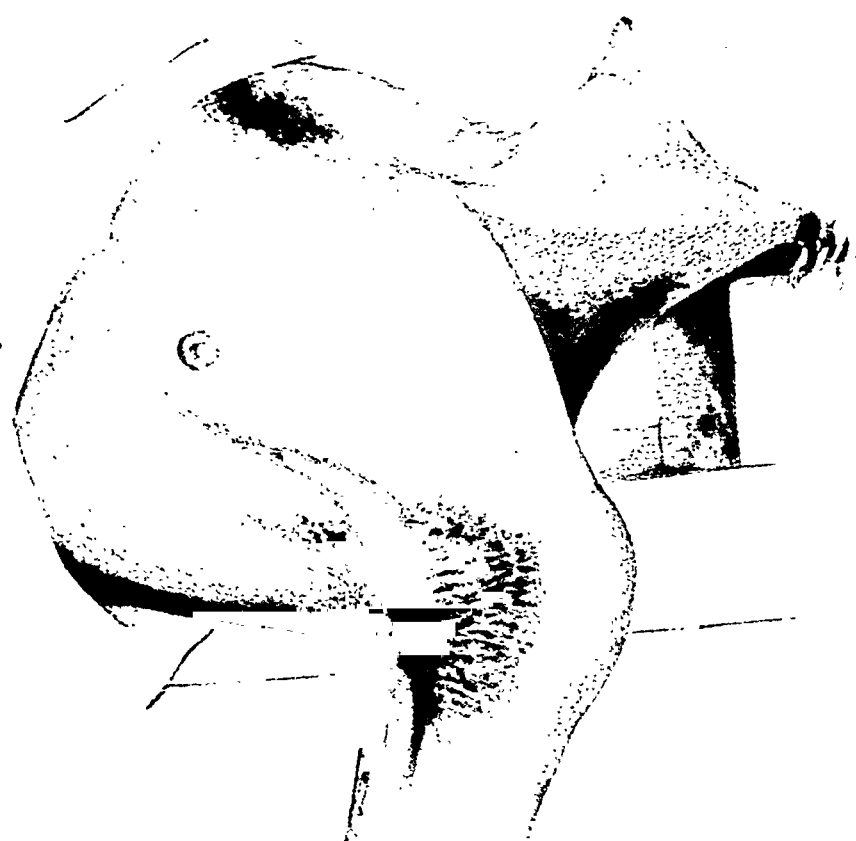


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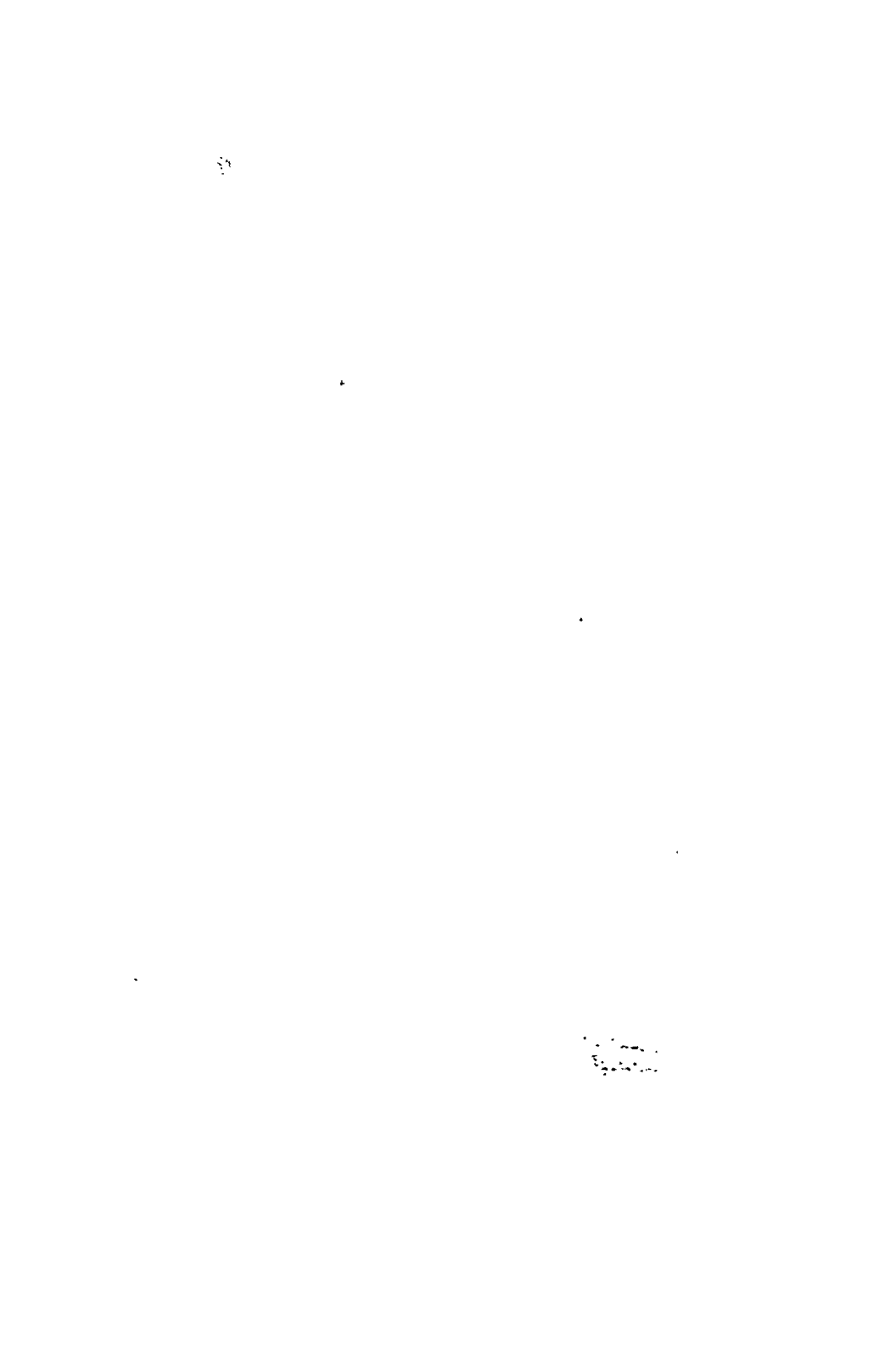
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WILLIAM WITHERING

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William Withering

BIOGRAPHY

- March 17, 1741. Born at Wellington in Shropshire, England, son of Edmund Withering, a physician, and of Sarah Hector, his wife. Received a classical education from a neighboring clergyman, the Reverend Henry Wood of Ercall.
- 1762 Age 21. Entered the University of Edinburgh, studied under Alexander Monro, primus, Joseph Black, William Cullen and Robert Whytt.
- 1766 Age 25. Graduated from Edinburgh with degree of "Doctor of Physic," his thesis being titled "Malignant Putrid Sore Throat." Traveled on the continent but had an unhappy time because of the illness and death of his companion. On returning home helped with his father's practice for a short time and then settled in nearby Stafford. Appointed first physician of the newly built Stafford Infirmary.
- 1767 Age 26. While practice was young and unhurried Withering gathered flowers to be painted by one of his patients, Helena Cook. She became his wife.
- 1772 Age 31. Married. Began to look for a practice with a larger income.
- 1775 Age 34. Moved to Birmingham where he was associated with Dr. John Ash of the General Hospital. The income of Stafford was doubled the first year in Birmingham.

- 1776 Age 35. Published his first book, "A botanical arrangement of all the vegetables naturally growing in Great Britain with descriptions of the genera and species according to Linnaeus." Continued studies on natural history and had an increasingly busy practice. Joined the Lunar Society of Birmingham, among its members being James Watt, Josiah Wedgewood, Dr. Erasmus Darwin and Joseph Priestley.
- 1783 Age 42. Had to give up practice for many months because of poor health (pulmonary tuberculosis). Spent his time in writing and translating; prepared manuscript on digitalis.
- 1785 Age 44. Sought as consultant over a wide area of middle and western England and Wales. In this year traveled 6,303 miles by horse and carriage to visit patients. Published "An account of the fox-glove." Elected a Fellow of the Royal Society and given a diploma of the Medical Society of London; both high honors. Withering's home at Edgbaston Hall was a mecca for most of the distinguished scientists of the day.
- 1790 Age 49. Elected a Fellow of the Linnaean Society. Suffered a serious attack of pleurisy.
- 1792 Age 51. Spent the winter in Portugal because of poor health; returned there for the winter of 1793.
- 1796 Age 55. Withering's health forced him to retire.
- 1799 Age 58. Died on October 6 of pulmonary tuberculosis. Buried in Edgbaston Church.

EPONYMS

WITHERITE: The natural barium carbonate, discovered by Withering and named in his honor by the German geologist Werner in 1790. The mineral is found in large deposits in crystalline form near Hexham, Northumberland, and is used in the manufacturing of plate glass and paint and in the refining of sugar.

WITHERINGIA: A genus of plants; term applied by the French botanist, L'Heritier de Brutelle.

BIBLIOGRAPHY OF WRITINGS

A—Army Medical Library.

B—New York Academy of Medicine Library.

C—Kings County Medical Society, Brooklyn, Library.

D—John Crerar Library, Chicago.

E—Lane Medical Library of Stamford University.

1. De angina gangraenosa. 31pp., 8°, Edinb., Auld & Smellie, 1766. In A and B.
2. Experiments upon the different kinds of marle found in Staffordshire. Phil. Trans. Roy. Soc., Lond., 63: 161–162. 1773.
3. A botanical arrangement of all the vegetables naturally growing in Great Britain with descriptions of the genera and species according to Linnaeus. 2 vols., 8°, 1776. Botanical arrangement of British plants. 2 ed., 3 vols., 8°, Birmingham, Robinson, 1787–1792. (Same) 3. ed., 4 vols., 8°, Birmingham, The author, 1796. In B. (Same) 4. ed., 4 vols., 8°, Lond., Cadell & Davies, 1801. In B. (Same) 6. ed., corrected and considerably enlarged by William Withering, Jr. 4 vols., 8°, Lond., Cadell & Davies, 1818. In B and C.
4. Contributed scientific notes to John Talbot Dillon's Travels through Spain, with a view to illustrate the natural history and physical geography of that kingdom, 1776.
5. An account of the scarlet fever and sore throat, or scarlatina anginosa; particularly as it appeared at Birmingham in the year 1778. 132 pp., 8°, Lond., 1779. In A. (Same) In German. Beschreibung des mit einem wehen Hals verknüpften Scharlachfiebers, sowie dasselbe besonders im Jahre 1778 zu Birmingham in England erschien. Aus dem Englishcen übersetzt und mit einigen Anmerkungen und Zusäzen versehen von J. A. J. Sauer. 3 pl., 136 pp., 12°, Frankfurt a. M., J. G. Garhe, 1781. In A. (Same) 2. ed. To which are now prefixed some remarks

- on the nature and cure of the ulcerated sore throat. 127 pp., 8°, Birmingham, Robinson, 1793. In A, B, C, and E.
6. An analysis of two mineral substances, viz., the Rowley-ragstone and the toad-stone. *Phil. Trans. Roy. Soc.*, Lond., 72: 327-336, 1782.
 7. Experiments and observations on the *Terra pondorsa*. *Ibid.*, 74: 293-311, 1784.
 8. An account of the fox-glove, and some of its medical uses; with practical remarks on dropsy and other diseases. xx, 207 pp., 1 p., 8°, Birmingham, Robinson, 1785. In A, B and D.
(Same) In German. *Abhandlung vom rothen Fingerhut und dessen Anwendung in der praktischen Heilkunde vorzeulich bei der Wassersucht und einigen andern Krankheiten. Aus dem Englischen vom—Christian Friedrich Michaelis—Leipzig, In der Johann Gottfried Müllerschen Buchhandlung, 1786.* xxviii, 234 pp., 1 l., 1 fold. col. plate, 19.6 cm. In B and D.
(Same) In German. *Bericht über den Fingerhut und seine medizinische Anwendung mit praktischen Bemerkungen über Wassersucht und andere Krankheiten. Nach der englischen Ausgabe von 1785 ins Deutsche übertragen.* 209 pp., 1 pl., 8°, Mannheim, C. F. Boehringer & Soehne G. m. b. H., 1929. In A.
 9. Letter describing experience in effect of arsenic in the cure of intermittents. In *Thomas Fowler's Medical Reports*. Lond., Johnson, 1786.
 10. Letter to Joseph Priestley on acidity. *Phil. Trans. Roy. Soc.*, Lond., 78: 313-330, 1788.
 11. An account of some extraordinary effects of lightning. *Ibid.*, 80: 293-295, 1790.
 12. Letters from Dr. Withering. By Thomas Beddoes. (Describes Withering's views on tuberculosis). 8°, Bristol, 1794. In A.
 13. Chemical analysis of the water at *Caldas da Rainha*. (In Portuguese and English.) 8°, 1795.
 14. The miscellaneous tracts of the late William Withering. To

which is prefixed a memoir of his life, character and writings by the editor, W. Withering, Jr., with meteorological and thermometrical observations at Edgbaston, etc. 2 vols., vi, 496 pp., port., iv., 503 pp., 8°, London, Longman, 1822. In A and E.

BIBLIOGRAPHY OF BIOGRAPHIES

- Biography by W. Withering, Jr. In Miscellaneous tracts of the late William Withering. 8°, London, 1822, 1: 1-209.
- Biography by G. S. Boulger. Dict. Nat. Biog., Lond., 62: 268-270, 1900.
- William Withering and his book on the fox-glove. By Louis Kolipinski. Med. Record, 86: 8-14, 1914.
- Also: 22 pp., 1 l., 12°, N. Y., 1914.
- Biography by A. R. Cushny. Proc. Roy. Soc. Med., Lond., 8, Sect. Hist. Med., 85-94, 1915.
- William Withering. By Eli Moschcowitz. Med. Pickwick, 1: 62-64, 1915.
- Biography by G. M. Fay. Med. Press & Circ., Lond., 100: 39, 1915; 103: 208, 1917.
- The pioneer in digitalis therapy and the prophet of intravenous medication. Med. Times, N. Y., 46: 267, 1918.
- Niederlandische Reichsinstitutes für pharmakotherapeutische Untersuchungen. Die Digitalis, 1923.
- Photographs of digitalis growing and of the tomb of William Withering. By F. A. Smith. Minneapolis, 1925. 2 pl. and letter in 4° envelope. In B.
- Biography. Medical Life, 33: 424, 1926.
- Biography by W. H. Wynn. Birmingham Med. Rev., n.s. 1: 45-63, 1926.
- The Withering letters in the possession of The Royal Society of Medicine. By Sir W. Hale-White. Proc. Roy. Soc. Med. Lond., 22: Sect. Hist. Med., 37-41, 1928-29.
- Letters and papers . . . presented to Yale University Library by Mrs. Edward S. Harkness, edited by Isabel M. Calder. By Ezra Stiles. x, 123 pp., 26 cm., New Haven, Yale Univ. Press, 1933. In B.

Withering on digitalis. By Wilfred T. Dawson and John Chapman. *Ann. Med. Hist.*, 6: 31-34, 1934.

William Withering. The introduction of digitalis into medical practice. By L. H. Roddis. *Ann. Med. Hist.*, 8: 93-112, 185-201, 1936.

Also, with additions, xi, 131 pp., 19.5 cm., N. Y., P. B. Hoeber, 1936.

INTRODUCTION

William Withering published his book "An account of the foxglove" in 1785. He tells us in his own words, however, that his attention was first drawn to the drug in 1775 when he was still in practice in Stafford and before he had moved to the bigger field of Birmingham. So we see that the work for which William Withering is now famous was begun and practically completed while he was a practitioner in a small town. He had settled in Stafford nine years before, shortly after having been graduated from the University of Edinburgh.

Withering wrote in the following manner:

"In the year 1775 my opinion was asked concerning a family recipe for the cure of dropsy. I was told that it had long been kept a secret by an old woman in Shropshire who had sometimes made cures after the more regular practitioners had failed. I was informed also that the effects produced were violent vomiting and purging; for the diuretic effects seemed to have been overlooked. This medicine was composed of twenty or more different herbs; but it was not very difficult for one conversant in these subjects to perceive that the active herb could be no other than foxglove."

The foxglove was included in the 1783 edition of the Edinburgh Pharmacopeia and its use quickly taken up by many doctors. As with most newly described medicines, this drug was used indiscriminately, in all types of diseases and in all manner of preparations and doses. A loud cry soon arose against this medicine. Withering recognized its true worth and determined to be its champion. He realized that if specific indications for digitalis could be described, if definite preparations and doses could be determined, the drug would have a very valuable place in medicine.

Withering expressed it thus:

"The use of the Foxglove is getting abroad and it is better the world should derive some information, however imperfect, from my experience, than that the lives of men should be hazarded by its unguarded exhibition, or that a medicine of so much efficacy should be condemned and rejected as dangerous and unmanageable."

Here was the man who, having sufficient scientific training and natural interest, seized upon the knowledge held by most of the countryfolk around Stafford that foxglove was effective against

dropsy. Most of the old wives of that district had added foxglove to the concoctions of herbs which they used for dropsical patients. Without great difficulty Withering determined that the active principle was the foxglove. Just as Jenner brought into the realm of science the countryman's knowledge of vaccination with cowpox against smallpox, so did Withering apply the layman's knowledge of the foxglove for dropsy.

The book which is here reproduced in its entirety is one of the great classics of medicine. Copies are rarely found on the open market and many of the largest medical libraries in the United States do not own one. L. H. Roddis tells us that to his knowledge the last one reported for sale appeared in 1932 for about \$262.50. To our knowledge the book has never been completely reproduced.

The original volume contains only 207 pages. Preface and introduction occupy pages v to xx. A beautiful plate is next inserted which is approximately twelve by seventeen inches in size. Withering had had the natural colors of the *Digitalis purpurea* reproduced because he feared that his readers might mistake other plants for the one he was describing. Pages 1 to 10 give an account of "The introduction of the foxglove into modern practice;" pages 10 to 108 contain an account of patients who were treated with digitalis. They represent many different types of disease and the author carefully indicates the result of his treatment. The remainder of the book is made up of the following important headings: communications from correspondents, pages 109-178; preparations and doses of the foxglove, 179-183; effects, rules and cautions, 184-188; constitution of patients, 189-192; practical remarks on dropsy, 193-207.

Withering sums up his knowledge of the use of digitalis in the following words:

"Let it be continued until it acts either on the kidneys, the stomach, the pulse, or the bowels; let it be stopped upon the first appearance of any one of these effects, and I will maintain that the patient will not suffer from its exhibition, nor the practitioner be disappointed in any reasonable effects."

We are deeply indebted to the Library of the New York Academy of Medicine for the use of their copy of Withering's book in the preparation of this volume.

A N
A C C O U N T
O F T H E
F O X G L O V E,
A N D

Some of its Medical Uses :

W I T H
PRACTICAL REMARKS ON DROPSY,
AND OTHER DISEASES.

B Y
WILLIAM WITHERING, M. D.
Physician to the General Hospital at Birmingham.

— *nonumque prematur in annum.*

HORACE.

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M,DCC,LXXXV.





An Account of the Foxglove, and Some of Its Medical Uses; With Practical Remarks on Dropsy, and Other Diseases

BY

WILLIAM WITHERING, M.D.

Physician to the General Hospital at Birmingham

PREFACE

AFTER being frequently urged to write upon this subject, and as often declining to do it, from apprehension of my own inability, I am at length compelled to take up the pen, however unqualified I may still feel myself for the task.

The use of the Foxglove is getting abroad, and it is better the world should derive some instruction, however imperfect, from my experience, than that the lives of men should be hazarded by its unguarded exhibition, or that a medicine of so much efficacy should be condemned and rejected as dangerous and unmanageable.

(p. vi) It is now about ten years since I first began to use this medicine. Experience and cautious attention gradually taught me how to use it. For the last two years I have not had occasion to alter the modes of management; but I am still far from thinking them perfect.

It would have been an easy task to have given select cases, whose successful treatment would have spoken strongly in favour

of the medicine, and perhaps been flattering to my own reputation. But Truth and Science would condemn the procedure. I have therefore mentioned every case in which I have prescribed the Foxglove, proper or improper, successful or otherwise. Such a conduct will lay me open to the censure of those who are disposed to censure, but it will meet the approbation of others, who are the best qualified to be judges.

To the Surgeons and Apothecaries, with whom I am connected in practice, both in this town and at a distance, I beg leave to (p. vii) make this public acknowledgment, for the assistance they so readily afforded me, in perfecting some of the cases, and in communicating the events of others.

The ages of the patients are not always exact, nor would the labour of making them so have been repaid by any useful consequences. In a few instances accuracy in that respect was necessary, and there it has been attempted; but in general, an approximation towards the truth, was supposed to be sufficient

The cases related from my own experience, are generally written in the shortest form I could contrive, in order to save time and labour. Some of them are given more in detail, when particular circumstances made such detail necessary; but the cases communicated by other practitioners, are given in their own words.

I must caution the reader, who is not a practitioner in physic, that no general deductions, decisive upon the failure or success (p. viii) of the medicine, can be drawn from the cases I now present to him. These cases must be considered as the most hopeless and deplorable that exist; for physicians are seldom consulted in chronic diseases, till the usual remedies have failed: and, indeed, for some years, whilst I was less expert in the management of the *Digitalis*, I seldom prescribed it, but when the failure of every other method compelled me to do it; so that upon the whole, the instances I am going to adduce, may truly be considered as cases lost to the common run of practice, and only snatched from destruction, by the efficacy of the *Digitalis*; and this in so remarkable a manner, that, if the properties of that plant had not been discovered, by far the greatest part of these patients must have died.

There are men who will hardly admit of any thing which an author advances in support of a favorite medicine, and I allow they may have some cause for their hesitation; nor do I expect they will wave their usual modes of judging (p. ix) upon the present occasion. I could wish therefore that such readers would pass over what I have said, and attend only to the communications from correspondents, because they cannot be supposed to possess any unjust predilection in favour of the medicine: but I cannot advise them to this step, for I am certain they would then close the book, with much higher notions of the efficacy of the plant than what they would have learned from me. Not that I want faith in the discernment or in the veracity of my correspondents, for they are men of established reputation; but the cases they have sent me are, with some exceptions, too much selected. They are not upon this account less valuable in themselves, but they are not the proper premises from which to draw permanent conclusions.

I wish the reader to keep in view, that it is not my intention merely to introduce a new diuretic to his acquaintance, but one which, though not infallible, I believe to be much more certain than any other in present use.

(p. x) After all, in spite of opinion, prejudice, or error, Time will fix the real value upon this discovery, and determine whether I have imposed upon myself and others, or contributed to the benefit of science and mankind.

Birmingham, 1st July, 1785.

(p. xi) INTRODUCTION.

The Foxglove is a plant sufficiently common in this island, and as we have but one species, and that so generally known, I should have thought it superfluous either to figure or describe it; had I not more than once seen the leaves of Mullein* gathered for those of Foxglove. On the continent of Europe too, other species are found, and I have been informed that our species is very rare in some parts of Germany, existing only by means of cultivation in gardens.

* *Verbascum* of Linnaeus.

Our plant is the *Digitalis purpurea** of Linnaeus. It belongs to the 2d order of the 14th class, or the DIDYNAMIA ANGIOSPERMIA. The essential characters of the genus are, *Cup with 5 divisions. Blossom bell-shaped, bugling. Capsule egg-shaped, 2-celled.*—LINN.

DIGITALIS purpurea. Little leaves of the empalement egg-shaped, sharp. Blossoms blunt; the upper lip entire. LINN.

(p. xii) REFERENCES TO FIGURES. These are disposed in the order of comparative excellence.

Rivini monopet. 104.

Flora danica, 74, parts of fructification.

Tournefort Institutiones. 73, A, E, L, M.

Fuchsii Hist. Plant. 893, copied in

Tragi stirp. histor. 889.

J. Bauhini histor. Vol. ii. 812, 3, and

Lonicera 74, 1.

Blackwell. auct. 16.

Dodonaei pempt. stirp. hist. 169, reprinted in

Gerard emacul. 790, 1, and copied in

Parkinson Theatr. botanic. 653, 1.

Gerard, first edition, 646, 1.

Histor. Oxon. Morison. V. 8, row 1. 1.

Flor. danic. 74, the reduced figure.

Blossom. The bellying part on the inside sprinkled with spots like little eyes. *Leaves* wrinkled. LINN.

Blossom. Rather tubular than bell shaped, bulging on the under side, purple; the narrow tubular part at the base, white. *Upper lip* sometimes slightly cloven.

CHIVES. *Threads* crooked, white. *Tips* yellow.

POINTAL. *Seed-bud* greenish. *Honey-cup* at its base more yellow. *Summit* cloven.

S. VESS. *Capsule* not quite so long as the cup.

Root. Knotty and fibrous.

(p. xiii) *STEM.* About 4 feet high; obscurely angular; leafy.

* The trivial name *purpurea* is not a very happy one, for the blossoms though generally purple, are sometimes of a pure white.

LEAVES. Slightly but irregularly serrated, wrinkled; dark green above, paler underneath. *Lower leaves* egg-shaped; upper leaves spear-shaped. *Leaf-stalks* fleshy; bordered.

FLOWERS. Numerous, mostly growing from one side of the stem and hanging down one over another. *Floral-leaves* fitting, taper-pointed. The numerous purple blossoms hanging down, mottled within; as wide and nearly half as long as the finger of a common-sized glove, are sufficient marks whereby the most ignorant may distinguish this from every other British plant; and the leaves ought not to be gathered for use but when the plant is in blossom.

PLACE. Dry, gravelly or sandy soils; particularly on sloping ground. It is a biennial, and flowers from the middle of *June* to the end of *July*.

I have not observed that any of our cattle eat it. The root, the stem, the leaves, and the flowers have a bitter herbaceous taste, but I don't perceive that nauseous bitter which has been attributed to it.

This plant ranks amongst the LURIDAE, one of the Linnaean orders in a natural system. It has for congeners, NICOTIANA, ATROPA, HYOSCYAMUS, DATURA, SOLANUM, & c. so that from the knowledge we possess of the virtues of those plants, and reasoning from botanical analogy, we might be led to guess at something of its properties.

(p. xiv) I intended in this place to have traced the history of its effects in diseases from the time of Fuchsius, who first describes it, but I have been anticipated in this intention by my very valuable friend, Dr. Stokes of Stourbridge, who has lately sent me the following

HISTORICAL VIEW OF THE PROPERTIES OF DIGITALIS

Fuchsius in his *hist. stirp.* 1542, is the first author who notices it. From him it receives its name of DIGITALIS, in allusion to the German name of *Fingerhut*, which signifies a finger-stall, from the blossoms resembling the finger of a glove.

SENSIBLE QUALITIES. Leaves bitterish, very nauseous. LEWIS *Mat. med.* i. 342.

SENSIBLE EFFECTS. Some persons, soon after eating of a kind of omalade, into which the leaves of this, with those of several other plants, had entered as an ingredient, found themselves much indisposed, and were presently after attacked with vomitings. *DODONAEUS pempt. 170.*

It is a medicine which is proper only for strong constitutions, as it purges very violently, and excites excessive vomitings. *RAY. hist. 767.*

Boerhaave judges it to be of a poisonous nature, *hist. plant.* but Dr. Alston ranks it among those indigenous vegetables, "which, though now disregarded, (p. xv) are medicines of great virtue, and scarcely inferior to any that the Indies afford." *LEWIS. Mat. med. i. p. 343.*

Six or seven spoonfuls of the decoction produce nausea and vomiting, and purge; not without some marks of a deleterious quality. *HALLER hist. n. 330 from Aerial Inst. p. 49, 50.*

THE FOLLOWING IS AN ABRIDGED ACCOUNT OF ITS EFFECTS UPON TURKEYS

M. Salerne, a physician at Orleans, having heard that several turkey pouts had been killed by being fed with Foxglove leaves, instead of mullein, he gave some of the same leaves to a large vigorous turkey. The bird was so much affected that he could not stand upon his legs, he appeared drunk, and his excrements became reddish. Good nourishment restored him to health in eight days.

Being then determined to push the experiment further, he chopped some more leaves, mixed them with bran, and gave them to a vigorous turkey cock which weighed seven pounds. This bird soon appeared drooping and melancholy; his feathers stared, his neck became pale and retracted. The leaves were given him for four days, during which time he took about half a handful. These leaves had been gathered about eight days, and the winter was far advanced. The excrements, which are naturally (p. xvi) green and well formed, became, from the first, liquid and reddish, like those of a dysenteric patient.

The animal refusing to eat any more of this mixture which

had done him so much mischief, I was obliged to feed him with bran and water only; but notwithstanding this, he continued drooping, and without appetite. At times he was seized with convulsions, so strong as to throw him down; in the intervals he walked as if drunk; he did not attempt to perch, he uttered plaintive cries. At length he refused all nourishment. On the fifth or sixth day the excrements became as white as chalk; afterwards yellow, greenish, and black. On the eighteenth day he died, greatly reduced in flesh, for he now weighed only three pounds.

On opening him we found the heart, the lungs, the liver, and gall-bladder shrunk and dried up; the stomach was quite empty, but not deprived of its villous coat. *Hist. de l'Academ. 1748. p. 84.*

EPILEPSY.—“It hath beene of later experience found also to be effectual against the falling sickness, that divers have been cured thereby; for after taking of the *Decoct. manipulor. ii. c. polypod. quercin. contus. oz. iv. in cerevisia*, they that have been troubled with it twenty-six years, and have fallen once in a weeke, or two or three times in a moneth, have not fallen once in fourteen or fifteen moneths, that is until the writing hereof.” *Parkinson, p. 654.*

(p. xvii) SCROPHULA.—“The herb bruised, or the juice made up into an ointment, and applied to the place, hath been found by late experience to be availeable for the King’s Evill.” *PARK. p. 654.*

Several hereditary instances of this disease said to have been cured by it. AERIAL INFLUENCES, *p. 49, 50*, quoted by *HALLER, hist. n. 330.*

A man with *scrophulous ulcers* in various parts of the body, and which in the right leg were so virulent that its amputation was proposed, cured by *fucc. express. cochl. i. bis intra xiv. dies, in ½ pinta cerevisiae calidae.*

The leaves remaining after the pressing out of the juice, were applied every day to the ulcers. *Pract. ess. p. 40* quoted by *MURRAY apparat. medicam. i. p. 491.*

A young woman with a *scrophulous tumour* of the eye, a re-

markable *swelling of the upper lip, and painful tumours of the joints of the fingers*, much relieved; but the medicine was left off, on account of its violent effects on the constitution. *Ib. p. 42* quoted as above.

A man with a *scrophulous tumour of the right elbow*, attended for three years *with excruciating pains*, was nearly cured by four doses of the juice taken once a month. *Ib. p. 43.* as above.

The physicians and surgeons of the Worcester Infirmary have employed it in ointments and poultices with remarkable efficacy. *Ib. p. 44.* It was recommended (p. xviii) to them by Dr. Baylies of Evesham, now of Berlin, as a remedy for this disease. Dr. Wall gave it a tryal, as well externally as internally, but their experiments did not lead them to observe any other properties in it, than those of a highly nauseating medicine and drastic purgative.

WOUNDS. In considerable estimation for the healing all kinds of wounds, *Lobel. adv. 245.*

Principally of use in ulcers, which discharge considerably, being of little advantage in such as are dry. HULSE, in R. hist. 768.

DOCTOR BAYLIES, physician to his Prussian Majesty, informed me, when at Berlin, that he employed it with great success in caries, and obstinate sore legs.

DYSPNOEA *Pituitosa* Sauvages i. 657.—“Boiled in water or wine, and drunken doth cut and consume the thicke toughnesse of grosse, and slimie flegme, and naughtie humours. The same, or boiled with honied water or sugar, doth scoure and clense the brest, ripeneth and bringeth foorth tough and clammie flegme. It openeth also the stoppage of the liver spleene and milt, and of the inwarde parts.” GERARDE hist. ed. l. p. 647.

Whensoever there is need of a rarefying or extenuating of tough flegme or viscous humours troubling the chest,—the decoction or juice hereof made up with sugar or honey is availeable, as also to clense and purge the body both upwards (p. xix) and downwards sometimes, of tough flegme, and clammy humours, notwithstanding that these qualities are found to bee in it, there are but few physitions in our times that put it to these uses, but it is in a manner wholly neglected.” PARKINSON, p. 654.

Previous to the year 1777, you informed me of the great success you had met with in curing dropsies by means of the fol. Digitalis, which you then considered as a more certain diuretic than any you had ever tried. Some time afterwards, Mr. Russel, surgeon, of Worcester, having heard of the success which had attended some cases in which you had given it, requested me to obtain for him any information you might be inclined to communicate respecting its use. In consequence of this application, you wrote to me in the following terms.*

In a letter which I received from you in London, dated *September* 29, 1778, you write as follows:—"I wish it was as easy to write upon the Digitals—I despair of pleasing myself or instructing others, in a subject so difficult. It is much easier to write upon a disease than upon a remedy. The former is in the hands of nature, and a faithful observer, with an eye of tolerable judgment, cannot fail to delineate a likeness. The latter will ever be subject to the whims, the inaccuracies, and the blunders of mankind."—

(p. xx) In my notes I find the following memorandum—"February 20th, 1779, gave an account of Doctor Withering's practice, with the precautions necessary to its success, to the Medical Society at Edinburgh."—In the course of that year, the Digitalis was prescribed in the Edinburgh Infirmary, by Dr. Hope, and in the following year, whilst I was Clerk to Dr. Home, as Clinical Professor, I had a favourable opportunity of observing its sensible effects.

In one case in which it was given properly at first, the urine began to flow freely on the second day. On the third, the swellings began to subside. The dose was then increased more than *quadruple* in the twenty-four hours. On the fifth day sickness came on, and much purging, but the urine still increased though the pulse sunk to 50. On the 7th day, a *quadruple* dose of the infusion was ordered to be taken every third hour, so as to bring on nausea again. The pulse fell to forty-four, and at length to thirty-five in a minute. The patient gradually sunk and died on the sixteenth day; but previous to her death, for two or three days, her pulse rose to near one hundred.—It is

* See the extract from this letter at page 5.

needless to observe to you, how widely the treatment of this case differed from the method which you have found so successful.

OF THE PLATE

The figure of the Foxglove, facing the Title Page, is copied by the permission and under the inspection of Mr. Curtis, from his admirable work, entitled *FLORA LONDINENSIS*. The accuracy of the drawings, the beauty of the colouring, the full descriptions, the accurate specific distinctions, and the uses of the different plants, cannot fail to recommend that work to the patronage of all who are interested in the encouragement of genius, or the promotion of useful knowledge.

Explanation

Fig. 1. The Empalement.

Fig. 2, 3, 4. Four Chives two long and two short, Tips at first large, turgid, oval, touching at bottom, of a yellowish colour, and often spotted; lastly changing both their form and situation in a singular manner.

Fig. 5, 6, 7. Seed-bud rather conical, of a yellow green colour. *Shaft* simple. *Summit* cloven.

Fig. 8. *Honeycup* a gland, surrounding the bottom of the Seed-bud.

Fig. 9. Seed-vessel, a pointed oval *capsule*, of two cells and two valves, the lowermost valve splitting in two.

Fig. 10. Seeds numerous, blackish, small, lopped at each end.

AN ACCOUNT OF THE INTRODUCTION OF FOXGLOVE INTO MODERN PRACTICE

As the more obvious and sensible properties of plants, such as colour, taste, and smell, have but little connexion with the diseases they are adapted to cure; so their peculiar qualities have no certain dependence upon their external configuration. Their chemical examination by fire, after an immense waste of time and labour, having been found useless, is now abandoned by general consent. Possibly other modes of analysis will be found out,

which may turn to better account; but we have hitherto made only a very small progress in the chemistry of animal and vegetable substances. Their virtues must therefore be learnt, either from observing their effects upon insects and quadrupeds; from analogy, deduced from the already known powers of some of their congenera, or from the empirical usages and experience of the populace.

The first method has not yet been much attended to; and the second can only be perfected in proportion as we approach towards the discovery of a truly natural system; but the last, as far as it extends, lies (p. 2) within the reach of every one who is open to information, regardless of the source from whence it springs.

It was a circumstance of this kind which first fixed my attention on the Foxglove.

In the year 1775, my opinion was asked concerning a family receipt for the cure of the dropsy. I was told that it had long been kept a secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed. I was informed also, that the effects produced were violent vomiting and purging; for the diuretic effects seemed to have been overlooked. This medicine was composed of twenty or more different herbs; but it was not very difficult for one conversant in these subjects, to perceive, that the active herb could be no other than the Foxglove.

My worthy predecessor in this place, the very humane and ingenious Dr. Small, had made it a practice to give his advice to the poor during one hour in a day. This practice, which I continued until we had an Hospital opened for the reception of the sick poor, gave me an opportunity of putting my ideas into execution in a variety of cases; for the number of poor who thus applied for advice, amounted to between two and three thousand annually. I soon found the Foxglove to be a very powerful diuretic; but then, and for a considerable time afterwards, I gave it in doses very much too (p. 3) large, and urged its continuance too long; for misled by reasoning from the effects of the squill, which generally acts best upon the kidneys when it

excites nausea, I wished to produce the same effect by the Foxglove. In this mode of prescribing, when I had so many patients to attend to in the space of one, or at most of two hours, it will not be expected that I could be very particular, much less could I take notes of all the cases which occurred. Two or three of them only, in which the medicine succeeded, I find mentioned amongst my papers. It was from this kind of experience that I ventured to assert, in the Botanical Arrangement published in the course of the following spring, that the *Digitalis purpurea* "merited more attention than modern practice bestowed upon it."

I had not, however, yet introduced it into the more regular mode of prescription; but a circumstance happened which accelerated that event. My truly valuable and respectable friend, Dr. Ash, informed me that Dr. Cawley, then principal of Brazen Nose College, Oxford, had been cured of a *Hydrops Pectoris*, by an empirical exhibition of the root of the Foxglove, after some of the first physicians of the age had declared they could do no more for him. I was now determined to pursue my former ideas more vigorously than before, but was too well aware of the uncertainty which must attend on the exhibition of the *root* of a *biennial* plant, and therefore continued to use the *leaves*. These I had found to vary much as to dose, at different seasons of the year; (p. 4) but I expected, if gathered always in one condition of the plant, viz. when it was in its flowering state, and carefully dried, that the dose might be ascertained as exactly as that of any other medicine; or have I been disappointed in this expectation. The more I saw of the great powers of this plant, the more it seemed necessary to bring the doses of it to the greatest possible accuracy. I suspected that this degree of accuracy was not reconcileable with the use of a *decoction*, as it depended not only upon the care of those who had the preparation of it, but it was easy to conceive from the analogy of another plant of the same natural order, the tobacco, that its active properties might be impaired by long boiling. The decoction was therefore discarded, and the *infusion* substituted in its place. After this I began to use the leaves in *powder*, but I still very often prescribe the infusion.

Further experience convinced me, that the *diuretic* effects of this medicine do not at all depend upon its exciting a nausea or vomiting; but, on the contrary, that though the increased secretion of urine will frequently succeed to, or exist along with these circumstances, yet they are so far from being friendly or necessary, that I have often known the discharge of urine checked, when the doses have been imprudently urged so as to occasion sickness.

If the medicine purges, it is almost certain to fail in its desired effect; but this having been the case, I have seen it afterwards succeed when joined with (p. 5) small doses of opium, so as to refrain its action on the bowels.

In the summer of the year 1776, I ordered a quantity of the leaves to be dried, and as it then became possible to ascertain the doses, it was gradually adopted by the medical practitioners in the circle of my acquaintance.

In the month of *November* 1777, in consequence of an application from that very celebrated surgeon, Mr. Russel, of Worcester, I sent him the following account, which I choose to introduce here, as shewing the ideas I then entertained of the medicine, and how much I was mistaken as to its real dose.—

“I generally order it in decoction. Three drams of the dried leaves, collected at the time of the blossoms expanding, boiled in twelve to eight ounces of water. Two spoonfuls of this medicine, given every two hours, will sooner or later excite a nausea. I have sometimes used the green leaves gathered in winter, but then I order three times the weight; and in one instance I used three ounces to a pint decoction, before the desired effect took place. I consider the Foxglove thus given, as the most certain diuretic I know, nor do its diuretic effects depend merely upon the nausea it produces, for in cases where squill and ipecac have been so given as to keep up a nausea several days together, and the flow of urine not taken place, I have found the Foxglove to succeed; and I have, in more than one instance, given the Foxglove in smaller and (p. 6) more distant doses, so that the flow of urine has taken place without any sensible affection of the stomach; but in general I give it in the manner first mentioned, and order one dose to be taken after the sickness commences, I

then omit all medicines, except those of the cordial kind are wanted, during the space of three, four, or five days. By this time the nausea abates, and the appetite becomes better than it was before. Sometimes the brain is considerably affected by the medicine, and indistinct vision ensues, but I have never yet found any permanent bad effects from it.

"I use it in the Ascites, Anasarca, and Hydrops Pectoris; and so far as the removal of the water will contribute to cure the patient, so far may be expected from this medicine: but I wish it not to be tried in ascites of female patients, believing that many of these cases are dropsies of the ovaria; and no sensible man will ever expect to see these encysted fluids removed by any medicine.

"I have often been obliged to evacuate the water repeatedly in the same patient, by repeating the decoction; but then this has been at such distances of time as to allow of the interference of other medicines and a proper regimen, so that the patient obtains in the end a perfect cure. In these cases the decoction becomes at length so very disagreeable, that a much smaller quantity will produce the effect, and I often find it necessary to alter its taste by the addition of Aq. Cinnam. sp. or Aq. Juniper. composita."

(p. 7) "I allow, and indeed enjoin my patients to drink very plentifully of small liquors through the whole course of the cure; and sometimes, where the evacuations have been very sudden, I have found a bandage as necessary as in the use of the trochar."—

Early in the year 1779, a number of dropsical cases offered themselves to my attention, the consequences of the scarlet fever and sore throat which had raged so very generally amongst us in the preceding year. Some of these had been cured by squills or other diuretics, and relapsed; in others, the dropsy did not appear for several weeks after the original disease had ceased: but I am not able to mention many particulars, having omitted to make notes. This, however, is the less to be regretted, as the symptoms in all were very much alike, and they were all without exception cured by the Foxglove.

This last circumstance encouraged me to use the medicine more

frequently than I had done heretofore, and the increase of practice had taught me to improve the management of it.

In *February* 1779, my friend, Dr. Stokes, communicated to the Medical Society at Edinburgh the result of my experience of the Foxglove; and, in a letter addressed to me in *November* he says, "Dr. Hope, in consequence of my mentioning its use to my friend, Dr. Broughton, has tried the Foxglove in the Infirmary with success." Dr. (p. 8) Stokes also tells me that Dr. Hamilton cured Dropsies with it in the year 1781.

I am informed by my very worthy friend Dr. Duncan, that Dr. Hamilton, who learnt its use from Dr. Hope, has employed it very frequently in the Hospital at Edinburgh. Dr. Duncan also tells me, that the late very ingenious and accomplished Mr. Charles Darwin, informed him of its being used by his father and myself, in cases of Hydrothorax, and that he has ever since mentioned it in his lectures, and sometimes employed it in his practice.

At length, in the year 1783, it appeared in the new edition of the Edinburgh Pharmacopoeia, into which, I am told, it was received in consequence of the recommendation of Dr. Hoppe. But from which, I am satisfied, it will be again very soon rejected, if it should continue to be exhibited in the unrestrained manner in which it has heretofore been used at Edinburgh, and in the enormous doses in which it is now directed in London.

In the following cases the reader will find other diseases besides dropsies; particularly several cases of consumption. I was induced to try it in these, from being told, that it was much used in the West of England, in the Phthisis Pulmonalis, by the common people. In this disease, however, in my hands, it has done but little service, and yet I am disposed to wish it a further trial, for in a copy of Parkinson's Herbal, which I saw about two years ago, (p. 9) I found the following manuscript note at the article *Digitalis*, written, I believe, by a Mr. Saunders, who practiced for many years with great reputation as a surgeon and apothecary at Stourbridge, in Worcestershire.

"Consumptions are cured infallibly by weak decoction of Foxglove leaves in water, or wine and water, and drank for constant drink. Or take of the juice of the herb and flowers, clarify

it, and make a fine syrup with honey, of which take three spoonfuls thrice in a day, at physical hours. The use of these two things of late has done, in consumptive cases, great wonders. But be cautious of its use, for it is of a vomiting nature. In these things begin sparingly, and increase the dose as the patient's strength will bear, least, instead of a sovereign medicine, you do real damage by this infusion or syrup."

The precautions annexed to his encomiums of this medicine, lead one to think that he has spoken from his own proper experience.

I have lately been told, that a person in the neighbourhood of Warwick, possesses a famous family receipt for the dropsy, in which the Foxglove is the active medicine; and a lady from the western part of Yorkshire assures me, that the people in her country often cure themselves of dropsical complaints by drinking Foxglove tea. In confirmation of this, I recollect about two years ago being desired to visit a (p. 10) travelling Yorkshire tradesman. I found him incessantly vomiting, his vision indistinct, his pulse forty in a minute. Upon enquiry it came out, that his wife had stewed a large handful of green Foxglove leaves in half a pint of water, and given him the liquor, which he drank at one draught, in order to cure him of an asthmatic affection. This good woman knew the medicine of her country, but not the dose of it, for her husband narrowly escaped with his life.

It is probable that this rude mode of exhibiting the Foxglove has been more general than I am at present aware of; but it is wonderful that no author seems to have been acquainted with its effects as a diuretic.

CASES IN WHICH THE DIGITALIS WAS GIVEN BY THE DIRECTION
OF THE AUTHOR

1775

It was in the course of this year that I began to use the Digitals in dropsical cases. The patients were such as applied at my house for advice gratis. I cannot pretend to charge my memory with particular cases, or particular effects, and I had not leisure

to make notes. Upon the whole, however, it may be concluded, that the medicine was found useful, or I should not have continued to employ it.

Case I

December 8th. A man about fifty years of age, who had formerly been a builder, but was now much reduced in his circumstances, complained to me of an asthma which first attacked him about the latter end of autumn. His breath was very short, his countenance was sunken, his belly large; and, upon examination, a fluctuation in it was very perceptible. His urine for some time past had been small in quantity. I directed a decoction of Fol. Digital. recent, which made him very sick, the sickness recurring at intervals for several days, during which time he made a large quantity of water. His breath gradually drew easier, his belly subsided, and in (p. 12) about ten days he began to eat with a keen appetite. He afterwards took steel and bitters.

1776

Case II

January 14th. A poor man labouring under an ascites and anasarca, was directed to take a decoction of Digitalis every four hours. It purged him smartly, but did not relieve him. An opiate was now ordered with each dose of the medicine, which then acted upon the kidneys very freely, and he soon lost all his complaints.

Case III

March 15th. A poor boy, about nine years of age, was brought for my advice. His countenance was pale, his pulse quick and feeble, his body greatly emaciated, except his belly, which was very large, and, upon examination, contained a fluid. The case had been considered as arising from worms. He was directed to take the decoction of Digitalis night and morning. It operated as a diuretic, never made him sick, and he got well without any other medicine.

Case IV

July 25th. Mrs. H—, of A—, near N—, between forty and fifty years of age, a few weeks ago, after some previous indisposition, was attacked by a severe cold shivering fit, succeeded by fever; great pain in her left side, shortness of breath, perpetual cough, and, after some days, (p. 13) copious expectoration. On the 4th of *June*, Dr. Darwin,* was called to her. I have not heard what was then done for her, but between the 15th of *June*, and 25th of *July*, the Doctor, at his different visits, gave her various medicines of the deobstruent, tonic, antispasmodic, diuretic, and evacuant kinds.

On the 25th of *July* I was desired to meet Dr. Darwin at the lady's house. I found her nearly in a state of suffocation; her pulse extremely weak and irregular, her breath very short and laborious, her countenance sunk, her arms of a leaden colour, clammy and cold. She could not lye down in bed, and had neither strength nor appetite, but was extremely thirsty. Her stomach, legs, and thighs were greatly swollen; her urine very small in quantity, not more than a spoonful at a time, and that very seldom. It had been proposed to scarify her legs, but the proposition was not acceded to.

She had experienced no relief from any means that had been used, except from ipecacoanha vomits; the dose of which had been gradually increased from 15 to 40 grains, but such was the insensible state of her stomach for the last few days, that even those very large doses failed to make her sick, and consequently purged her. In this situation of things I knew of nothing likely to avail us, except the *Digitalis*: but this I hesitated to propose, from an apprehension that little could be expected from any thing; that an unfavourable termination would tend to (p. 14) discredit a medicine which promised to be of great benefit to mankind, and I might be censured for a prescription which could not be countenanced by the experience of any other regular practitioner. But these considerations soon gave way to the desire of preserving the life of this valuable woman, and accord-

* Then resident at Lichfield, now at Derby.

ingly I proposed the *Digitalis* to be tried; adding, that I sometimes had found it to succeed when other, even the most judicious methods, had failed. Dr. Darwin very politely, acceded immediately to my proposition and, as he had never seen it given, left the preparation and the dose to my direction. We therefore prescribed as follows:

R. Fol. Digital. purp. recent. oz. iv. coque ex Aq. fontan. purae lb iss ad lb i. et cola.

R. Decoct. Digital. oz. iss.

Aq. Nuc. Moschat. oz. ii. M. fiat, haust. 2dis horis sumend.

The patient took five of these draughts, which made her very sick, and acted very powerfully upon the kidneys, for within the first twenty-four hours she made upwards of eight quarts of water. The sense of fulness and oppression across her stomach was greatly diminished, her breath was eased, her pulse became more full and regular, and the swellings of her legs subsided.

26th. Our patient being thus snatched from impending destruction, Dr. Darwin proposed to give her a decoction of *pareira brava* and *guaiacum* shavings, (p. 15) with pills of myrrh and white vitriol; and, if costive, a pill with calomel and aloes. To these propositions I gave a ready assent.

30th. This day Dr. Darwin saw her, and directed a continuation of the medicines last prescribed.

August 1st. I found the patient perfectly free from every appearance of dropsy, her breath quite easy, her appetite much improved, but still very weak. Having some suspicion of a diseased liver, I directed pills of soap, rhubarb, tartar of vitriol, and calomel to be taken twice a day, with a neutral saline draught.

9th. We visited our patient together, and repeated the draughts directed on the 26th of *June*, with the addition of tincture of bark, and also ordering pills of aloes, *guaiacum*, and *sal martis* to be taken if costive.

September 10th. From this time the management of the case fell entirely under my direction, and perceiving symptoms of effusion going forwards, I desired that a solution of *merc. subl.* corr. might be given twice a day.

19th. The increase of the dropsical symptoms now made it necessary to repeat the *Digitalis*. The dried leaves were used in infusion, and the water was presently evacuated, as before.

(p. 16) It is now almost nine years since the *Digitalis* was first prescribed for this lady, and notwithstanding I have tried every preventive method I could devise, the dropsy still continues to recur at times; but is never allowed to increase so as to cause much distress, for she occasionally takes the infusion and relieves herself whenever she chooses. Since the first exhibition of that medicine, very small doses have been always found sufficient to promote the flow of urine.

I have been more particular in the narrative of this case, partly because Dr. Darwin has related it rather imperfectly in the notes to his son's posthumous publication, trusting, I imagine, to memory, and partly because it was a case which gave rise to a very general use of the medicine in that part of Shropshire.

Case V

December 10th. Mr. L—, Aet, 35. Ascites and anasarca, the consequence of very intemperate living. After trying squill and other medicines to no purpose, I directed a decoction of the *Fol. Digital. recent.* six drams to a pint; an eighth part to be taken every fourth hour. This made him sick, and produced a copious flow of urine, but not enough to remove all the dropsical symptoms. After a fortnight a stronger decoction was ordered, and upon a third trial, as the winter advanced, it became necessary to use four ounces to the pint decoction; and thus he got free from all his complaints.

(p. 17) In *October* 1777, in consequence of having pursued his intemperate mode of living, his dropsy returned, accompanied by evident marks of diseased viscera. A decoction of two drams of *Fol. Digital. sicc.* to a pint, once more removed the dropsy. He took a wine glass full thrice a day.

In *January* 1778, I was desired to visit him again. I found he had gone on in his usual intemperate life, his countenance jaundiced, and the dropsy coming on apace. After giving some deobstruent medicines, I again directed the *Digitalis*, which again emptied the water; but he did not survive many weeks.

1777

Case VI

February —. Mrs. M——, Aet. 45. Ascites and anasarca, but not much otherwise diseased, and well enough to walk about the house, and see after her family affairs. I thought this a fair case for a trial of the *Digitalis*, and therefore directed a decoction of the fresh leaves, the stock of dried ones being exhausted. About a week afterwards, calling to see my patient, I was informed that she was dead; that the third day after my first visit she suddenly fell down, and expired. Upon enquiry I found she had not taken any of the medicine; for the snow had lain so deep upon the ground, that the apothecary had not been able to procure it. Had (p. 18) the medicine been given in a case seemingly so favourable as this, and had the patient died under its use, is it not probable that the death would have been attributed to it?

Case VII

February 11th. Mr. E——, of W——. Aet. 61. Hydrothorax, ascites and anasarca, consequences of hard drinking. He had been attended for some time by a physician in his neighbourhood, who had treated his case with the usual remedies, but without affording him any relief; nor could I expect to succeed better by any other medicine than the *Digitalis*. The dried leaves were not to be had; and the green ones at this season being very uncertain in their strength, I ordered four ounces of the roots in a pint decoction, and directed three spoonfuls to be given every fourth hour, until it either excited nausea, or a free discharge of urine; both these effects took place nearly at the same time: he made a large quantity of water, the swellings subsided very considerably, and his breath became easy. Eight days afterwards he began upon a course of bitters and deobstruents. The dropsical symptoms soon increased again, but he had suffered so much from the severity of the sickness before, that he was neither willing to take, nor I to give the same medicine again.

Perhaps this patient might have been saved, if I had been well acquainted with the management and (p. 19) real doses of the

medicine, which was certainly in this instance made very much too strong; and notwithstanding the caution to stop the further exhibition when certain effects should take place, it seems the quantity previously swallowed was sufficient to distress him exceedingly.

Case VIII

March 11th. Mrs. H—, Aet. 32. A few days after a tedious labour, had her legs and thighs swelled to a very great degree; pale and semi-transparent,* with pain in both groins. After a purge of calomel and rhubarb, ung. merc. was ordered to be rubbed upon the groins, and the following decoction was directed:

R. Fol. Digital. purp. recent. oz. ii.

Aq. purae. lbi. coque ad lbiss et colatur. adde.

Aq. cinn. sp. oz. iv. M. capita. cyath. vinos. parv. bis quotidie.

The decoction presently increased the secretion of urine, and abated the distension of the legs: in a fortnight the swelling was gone; but some days after leaving her bed, her legs swelled again about the ancles, which was removed by another bottle of the decoction on the 21st of *April*.

(p. 20) Case IX

March 29th. Mr. G—, Aet. 47. Very much deformed; asthma of several years continuance, but now dropsical to a great degree. Took several medicines without relief, and then tried the *Digitalis*, but with no better success.

Case X

April 10th. G— G—, Aet. 70. Asthma and anasarca. Took a decoction of the fresh leaves of the *Digitalis*, which produced violent sickness, but no immediate evacuation of water. After the sickness had ceased altogether, the urine began to flow copiously, and he was cured.

* This disease has lately been well described by Mr. White, of Manchester.

Case XI

July 10th. Mr. M—— of T——, Aet. 54. A very hard drinker; had been affected since *November* last with ascites and anasarca, for which he had taken several medicines without benefit. A decoction of the recent leaves of the *Digitalis* was then directed, an ounce and half to a pint, one eighth of which I ordered to be given every fourth hour. A few doses brought on great nausea, indistinct vision, and a great flow of urine, so as presently to empty him of all the dropsical water. Indeed the evacuation was so rapid and so complete, that it became necessary to apply a bandage round the belly, and to support him with cordials.

(p. 21) In something more than a year and a half, his dropsy returned, but the *Digitalis* did not then succeed to our wishes. In *August*, 1779, he was tapped, and lived afterwards only about five weeks.

For more particulars, see the extract of a letter from Mr. Lyon.

Case XII

September 12th. Miss C—— of T——, Aet. 48. An ovarium dropsy, and anasarcaous legs and thighs. For three months in the beginning of this year she had been under the care of Dr. Darwin, who at different times had given her blue vitriol, elaterium, and calomel; decoction of *pareira brava*, and *guaiacum* wood, with tincture of *cantharides*; oxymel of squills, decoction of *parsley* roots, &c. Finding no relief, she discontinued the use of medicines, until the urgency of her symptoms induced her to ask my advice about the end of *August*. She was greatly emaciated, and had almost a total loss of appetite. I first tried small doses of *Merc. sublim. corr.* in solution, with decoction of *burdock* roots, and blisters to the thighs. No advantage attending the use of this plan, I directed a decoction of *Fol. Digit.* a dram and a half to a pint; one ounce to be taken twice a day. It presently reduced the anasarcaous swellings, but made no alteration in the distension of the abdomen.

(p. 22) *Case XIII*

October 9th. Mrs. B——, Aet. 40. An ovarium dropsy. Took a decoction of Digitalis without effect. Her life was preserved for some years by repeated tapping.

1778

Case XIV

February 8th. Mr. R—— of K——. Had formerly suffered much from gout, and lived very intemperately. Jaundiced countenance; ascites; legs and thighs greatly swollen; appetite none; extremely weak; confined to his bed. Had taken many medicines from his apothecary without advantage. I ordered him decoction of Digitalis, and a cordial; but he survived only a few days.

Case XV

March 13th. Mr. M——, Aet. 54. A thorax greatly deformed; asthma through the winter, succeeded by dropsy in belly and legs. Pulse very small; face leaden coloured; cough almost continual. Decoction of seneka was directed, and small doses of Dover's powder at night.

17th. Gum-ammoniac and squill, with elixir parego. at night. —26th, Squill and decoction of seneka.—30th. His complaints still increasing, decoction (p. 23) of Digitalis was then directed, which relieved him in a few days; but his complaints returned again, and he died in the month of *June*.

Case XVI

August 18th. Mr. B——, Aet. 33. Pulmonary consumption and dropsy. The Digitalis, and that failing, other diuretics were used, in hopes of gaining some relief from the distress occasioned by the dropsical symptoms, but none of them were effectual. He was then attended by another physician, and died in about two months.

Case XVII.

September 21st. Mrs. M—— W—— G——, Aet. 50. An ovarium dropsy. She took half a pint of Infus. Digitalis, which

made her sick, but did not increase the quantity of urine. She was afterwards relieved by tapping.

Case XVIII

October 28th. R—— W——, Aet. 33. Ascites and universal anasarca; countenance quite pale and bloated; appetite none, and the little food he forces down is generally rejected.

R. Fol. Digit. purp. siccat. iii.

Aq. bull. lbi. digere per horas duas, et colat. adde aq. junip. comp. oz. iii.

(p. 24) He was directed to take one ounce of this infusion every two hours until it should make him sick. This was on Wednesday. The fifth dose made him vomit. On Thursday afternoon he vomited again freely, without having taken any more of the medicine. On Friday and Saturday he made more water than he had done for a week before, and the swellings of his face and body were considerably abated. He was directed to omit all medicine so long as the urine continued to flow freely, and also to keep an account of the quantity he made in twenty-four hours.

These were his reports:

October 31st. Saturday, 5 half pints.

November 1st. Sunday, 6

2d. Monday, 8

3d. Tuesday, 8

4th. Wednesday, 7

5th. Thursday, 8

On Wednesday he began to purge, and the purging still continues, but his appetite is better than he has known it for a long time. No swelling remains but about his ancles, extending at night half way up his legs.

Omit all medicines at present.

7th. Saturday 7 $\frac{1}{4}$ half pints.

8th. Sunday, 8

9th. Monday, 6 $\frac{3}{4}$

10th. Tuesday, 6 $\frac{1}{2}$

11th. Wednesday, 6

12th. Thursday, 6 $\frac{1}{4}$

(p. 25) On Tuesday the 17th, some swelling still remained about his ancles, but he was in every other respect perfectly well.

He took a few more doses of the infusion, and no other medicine.

Case XIX

December 8th. W—— B——, Aet. 60. A hard drinker. Diseased viscera; ascites and anasarca. An infusion of *Digitalis* was directed, but it had no other effect than to make him sick.

1779

In the beginning of this year we had many dropsies in children, who had suffered from the Scarlatine Anginosa; they all yielded very readily to the *Digitalis*, but in some the medicine purged, and then it did not prove diuretic, nor did it remove the dropsy until opium was joined with it, so as to prevent it purging.—I did not keep notes of these cases, but I do not recollect a single instance in which the *Digitalis* failed to effect a cure.

Case XX

January 1st. Mr. H——. Hydrops Pectoris; legs and thighs prodigiously anasarca; a very distressing sense of fulness and tightness across his stomach; urine in small quantity; pulse intermitting; breath very short.

(p. 26) He had taken various medicines, and been blistered, but without relief. His complaints continuing to increase, I directed an infusion of *Digitalis*, which made him very sick; acted powerfully as a diuretic, and removed all his symptoms.

About three months afterwards he was out upon a journey, and, after taking cold, was suddenly seized with difficulty of breathing, and violent palpitation of his heart: he sent for me, and I ordered the infusion as before, which very soon removed his complaints. He is now active and well; but, whenever he takes cold, finds some return of difficult breathing, which he soon removes by a dose or two of the infusion.

Case XXI

January 5th. Mrs. M——, Aet. 69. Hydrothorax, (called asthma) ascites and anasarca. I directed an infusion of *Fol.*

Digital. siccāt. three drams to a pint; a small wine glass to be taken every third or fourth hour. It made her violently sick, acted powerfully as a diuretic, set her breath perfectly at liberty, and carried off the swelling of her legs; when she was nearly emptied, she became so languid, that I thought it necessary to order cordials, and a large blister to her back. Mr. Ward, who attended as her apothecary, tells me she had some return of her asthma in *June* and *October* following, which was each time removed by the same medicine.

(p. 27) *Case XXII*

January 11th. Mr. H—, Aet. 59. Ascites and general anasarca. A large corpulent man, and a hard drinker: he had repeatedly suffered under complaints of this kind, but had been always relieved by the judicious assistance of Dr. Ash. In the present instance, however, not finding relief as usual from the prescriptions of my worthy friend, he sent for me; after examining into his situation, and informing myself what had been done to relieve him, I was satisfied that the Digitalis was the only medicine from which I had any thing to hope. It was therefore directed; but another patient requiring my assistance at a distance from town, I desired he would not begin the medicine before I returned, which would be early on the third day; for I was well aware of the difficulties before me, and that he would inevitably sink under too rapid an evacuation of the water. On my return I was informed, that the preceding evening, as he sat on his chair, his head sunk upon his breast, and he died.

This case, as well as case VI. is mentioned with a view to demonstrate to younger practitioners, how sudden and unexpected the deaths of dropsical patients sometimes happen, and how cautious we should be in assigning causes for effects.

Case XXIII

August 31st. Mr. C—, Aet. 57. Diseased viscera, jaundice, ascites and anasarca. After trying (p. 28) calomel, saline draughts, jallap purges, chrystals of tartar, pills of gum ammoniac, squills, and soap, sal succini, eleterium, & c. infusion of

Digitalis was directed, which removed all his urgent symptoms, and he recovered a pretty good state of health.

Case XXIV

September 11th. I was desired to visit Mr. L——, Aet. 63; a middle sized man; rather thin; not habitually intemperate; found him in bed, where he had been for three days. He was in a state of furious insanity, and had been gradually losing his reason for ten days before, but was not outrageous the first week: his apothecary had given him ten grains of emetic tartar, a dram of ipecacoanha, and an ounce of tincture of jallap, in the space of a few hours, which scarcely made him sick, and only occasioned a stool or two upon enquiring into the usual state of his health, I was told that he had been troubled with some difficulty of breathing for thirty years past, but for the nine last years this complaint had increased, so that he was often obliged to sit up the greater part of the night; and, for the last year, the sense of suffocation was so great, when he lay down, that he often sat up for a week together. His father died of an asthma before he was fifty. A few years ago, at an election, where he drank more than usual, his head was affected as now, but in a slighter degree, and his asthmatic symptoms banished; and now, notwithstanding he has been several (p. 29) days in bed, he feels not the least difficulty in breathing.

Apprehending that the insanity might be owing to the same cause which had heretofore occasioned the asthma, and that this cause was water; I ordered a decoction of the Fol. siccat Digital. three drams to half a pint; three spoonfuls to be taken every third hour: the fourth dose made him sick; the medicine was then stopped; the sickness continued at intervals, more or less, for four days, during which time he made a great quantity of water, and gradually became more rational. On the fifth day his appetite began to return, and the sickness ceased, but the flow of urine still continued.

A week afterwards I saw him again, and examined him particularly; his head was then perfectly rational, appetite very good, breath quite easy, permitting him to lie down in bed without

inconvenience, makes plenty of water, coughs a little, and expectorates freely. He took no other medicine, except a little rhubarb when costive.

Case XXV

September 15th. Mr. J. R—, Aet. 50. Subject to an asthmatical complaint for more than twenty years, but was this year much worse than usual, and symptoms of dropsy appeared. In *July* he took G. ammon. squill and seneka, with infus. amarum and fossil alkaly. In *August* infusum amar. (p. 30) with vin. chalyb. and at bed-time pil. styr. and squill. His complaints increasing, the squill was pushed as far as could be borne, but without any good effect. *September 15th*, an infusion of *Digitalis* was directed, but he died the next morning.

Case XXVI

September 18th. Mrs. R—, Aet. 30. After a severe child-bearing, found both her legs and thighs swelled to the utmost stretch of the skin. They looked pale, and almost transparent. The case being similar to that related at No. VIII. I determined upon a similar method of treatment, but as this patient had an inflammatory sore throat also, I wished to get that removed first, and in three or four days it was done. I then directed an infusion of *Digitalis*, which soon increased the urinary secretion, and reduced the swellings, without any disturbance of her stomach.

A few days after quitting her bed and coming down stairs, some degree of swelling in her legs returned, which was removed by calomel, an opening electuary, and the application of rollers.

Case XXVII

October 7th. Mr. F—, a little man, with a spine and thorax greatly deformed; for more than a year past had complained of difficult respiration, and a sense of fulness about his stomach; these complaints increasing, his abdomen gradually enlarged, (p. 31) and a fluctuation in it became perceptible. He had no anasarca, no appearance of diseased viscera, and no great paucity

of urine. Purges and diuretics of different kinds affording him no relief, my assistance was desired. After trying squill medicines without effect, he was ordered to take Pulv. fol. Digital. in small doses. These producing no sensible effect, the doses were gradually increased until nausea was excited; but there was no alteration in the quantity of urine, and consequently no relief to his complaints. I then advised tapping, but he would not hear of it; however, the distress occasioned by the increasing fulness of his belly at length compelled him to submit to the operation on the 20th of *November*. It was necessary to draw off the water again upon the following days:

December the 8th.
 — — 27th.
 1780. *February* the 4th.
 — — 23rd.
 March the 9th.

During the intervals, no method I could think of was omitted to prevent the return of the disease, but nothing seemed to avail. In the operation of *February* 23rd, his strength was so much reduced, that the water was not entirely removed; and on the 9th of *March*, before his belly was half emptied, notwithstanding, the most judicious application of bandage, his debility was so great, that it was judged prudent to stop. After being placed in bed, the faintness and sickness continued; severe rigors (p. 32) ensued, and violent vomiting; these vomitings continued through the night, and in the intervals he lay in a state nearly approaching to syncope. The next day I found him with nearly the same symptoms, but remarked that the quantity of fluid he had thrown up was very much more than what he had taken, and that his abdomen was considerably fallen, in the course of two or three days more, he discharged the whole of the effused fluid, his strength and appetite gradually returned, and he was in all respects much better than he had been before the last operation.

Some time afterwards, his belly began to fill again, and he again applied to me; upon an accurate examination, I judged the quantity of fluid might then be about four or five quarts. Nature had pointed out the true method of cure in this case; I therefore

ordered him to bed, and directed ipecacoanha vomits to be given night and morning: in two or three days the whole of the water was removed by vomiting, for he never purged, nor was the quantity of his urine increased; his appetite and strength gradually returned; he never had any further relapse, and is now an active healthy man. I must leave the reader to make his own reflection on this singular case.

(p. 33) 1780

Case XXVIII

January 11th. Captain V—, Aet. 42. Had suffered much from residing in hot climates, and drinking very freely, particularly rum in large quantity. He had tried many physicians before I saw him, but nothing relieved him. I found him greatly emaciated, his countenance of a brownish yellow, no appetite, extremely low, distressing fulness across his stomach; legs and thighs greatly swollen; pulse quick, and very feeble; urine in small quantity. As he had evidently only a few days to live, I ordered him nothing but a solution of sal diureticus in cinnamon water, slightly acidulated with syrup of lemons. This medicine effecting no change, and his symptoms becoming daily more distressing, I directed an infusion of Digitalis. A few doses occasioned a copious flow of urine, without sickness or any other disturbance. The medicine was discontinued; and the next day the urine continuing to be secreted very plentifully, he lost his most distressing complaints, was in great spirits, and ate a pretty good dinner. In the evening, as he was conversing cheerfully with some friends, he stooped forwards, fell from his chair, and died instantly. Had he been in bed, I think there is reason to believe this fatal syncope, if such it was, would not have happened.

(p. 34) *Case XXIX*

February 6th. Mr. H—, Aet. 63. A corpulent man: had suffered much from gout, which for the last year or two had formed very imperfectly. He had now symptoms of water in

his chest, his belly and his legs. An infusion of Digitalis removed these complaints, and after being confined for the greater part of the winter, he was well enough to get abroad again. In the course of a month the dropsical symptoms returned, and were again removed by the same medicine. Bitters and tonics were now occasionally prescribed, but his debility gradually increased, and he died some time afterwards; but the dropsy never returned.

Case XXX

February 17th. Mr. D—, Aet. 50. Ascites and anasarca, with symptoms of phthisis. He had been a very hard drinker. The infusum Digitalis removed his dropsical symptoms, and he was sufficiently recovered to take a journey; but as the spring advanced, the consumptive symptoms increased, and he died soon afterwards, perfectly emaciated.

Case XXXI

March 5th. I was desired to visit Mrs. H—, a very delicate woman, who after a severe lying-in, had her legs and thighs swollen to a very great degree; (p. 35) pale and semi-transparent. I found her extremely faint, her pulse very small and slow; vomiting violently, and frequently purging. She was attended by a gentleman who had seen me give the Digitalis in a similar case of swelled legs after a lying-in (see Case XXVI.) about six months before. He had not considered that this patient was delicate, the other robust; nor had he attended to stop the exhibition of the medicine when its effects began to take place. The great distress of her situation was evidently owing to the imprudent and unlimited use of the Digitalis. I was very apprehensive for her safety; ordered her cordials and volatiles; a free supply of wine, chamomile tea with brandy for common drink, and blisters. The next day the situation of things was much the same, but with all this disturbance no increased secretion of urine. The same methods were continued; an opiate ordered at night, and liniment, volatile upon flannel applied to the groins, and she now complained of great pain in those parts. The third day the nausea was less urgent, the vomitings less frequent, the pulse

not so slow. Camphorated spirit, with caustic volatile alkaly, was applied to the stomach, emulsion given for common drink, and the same medicines repeated. From this time, the intervals became gradually longer between the fits of vomiting, the flow of urine increased, the swellings subsided, the appetite returned, and she recovered perfectly.

(p. 36) *Case XXXII*

March 16th. Mr. D—, Aet. 70. A paralytic stroke had for some weeks past impaired the use of his left side, and he complained much of his breath, and of a straitness across his stomach; at length, an anasarca and ascites appearing, I had no doubt as to the cause of the former symptoms; but, upon account of his advanced age, and the paralytic affection, I hesitated to give the *Digitalis*, and therefore tried the other usual modes of practice, until at length his breath would not permit him to lie down in bed, and his other symptoms increased so rapidly as to threaten a speedy dissolution. In this dilemma I ventured to prescribe an infusion of the *Fol. sicc. Digital.* which presently excited a copious flow of urine, and made him very sick; a strong infusion of chamomile flowers, with brandy, relieved the sickness, but the diuretic effects of the *Digitalis* continuing, his dropsy was removed, and his breathing became easy. The palsy remained nearly in the same state. He lived until *August 1782*, and without any return of the dropsy.

Case XXXIII

March 18th. Miss S—, Aet. 5. *Hydrocephalus internus.* As the case did not yield to calomel, when matters were nearly advanced to extremities, it occurred to me to try the *Infusum Digitalis*; a few doses of which were given, but had no sensible effect.

(p. 37) *Case XXXIV*

March 19th. A young lady, soon after the birth of an illegitimate child, became insane. After being nearly a month under my care, swellings of her legs, which at first had been attributed to weakness, extended to her thighs and belly; her urine became foul,

and small in quantity, and the insanity remained nearly the same. As it had been very difficult to procure evacuations by any means, I ordered half an ounce of Fol. Digital. siccat. in a pint infusion, and directed two spoonfuls to be given every two hours: this had the desired effect; the dropsy and the insanity disappeared together, and she had afterwards no other medicine but some aperient pills to take occasionally.

Case XXXV

April 12th. Mr. R—, Aet. 32. For the last three or four years had had more or less of what was considered as asthma;—it appeared to me Hydrothorax. I directed an infusion of Digitalis, which presently removed his complaints. In *June* following he had a relapse, and took two grains of Pulv. fol. Digit. three times a day, which cured him after taking forty grains, and he has never had a return.

(p. 38) Case XXXVI

May 15th. Mrs. H—, Aet. 40. A spasmodic asthma, attended with symptoms of effusion. An infusion of Digitalis relieved her very considerably, and she lived four years afterwards without any relapse.

Case XXXVII

May 26th. R—B—, Aet. 12. Scrophulus, consumptive, and at length anasarca. Took Infus. Digital, without advantage. Died the *July* following.

Case XXXVIII

June 4th. Mrs. S—, of W—, Aet. 49. Ascites and anasarca. Had taken many medicines; first from her apothecary, afterwards by the direction of a very judicious and very celebrated physician, but nothing retarded the increase of the dropsy. I first saw her along with the physician mentioned above, on the 14th of *May*; we directed an electuary of chrystals of tartar, and Seltzer water for common drink; this plan failing, as others had done before, we ordered the Infus. Digital. which in a few days

nearly removed the dropsy. I then left her to the care of her physician; but her constitution was too much impaired to admit of restoration to health, and I understand she died a few weeks afterwards.

(p. 39) *Case XXXIX*

June 13th. Mr. P—, Aet. 35. A very hard drinker, was attacked with a severe haemoptoe, which was followed by ascites and anasarca. He had every appearance of diseased viscera, and his urine was small in quantity. The power and the infusion of *Digitalis* were given at different times, but without the desired effect. Other medicines were tried, but in vain. Tapping prolonged his existence a few weeks, and he died early in the following autumn.

Case XL

June 27th. Mr. W—, Aet. 37. An apparently asthmatic affection, gradually increasing for three or four years, which not yielding to the usual remedies, he took the infusion of *Digitalis*. Two or three doses made him very sick; but he thought his breathing relieved. After one week he took it again, and was so much better as to want no other medicine.

In the course of the following winter he became hectic, and died consumptive about a year afterward.

Case XLI

July 6th. Mr. E—, Aet. 57. Hydrothorax and anasarca; his breath so short that he could not (p. 40) lie down. After a trial of squill, fixed alkaly, and dulcified spirit of nitre, I directed *Pulv. Digital. gr. 2*, thrice a day. In four days he was able to come down stairs; in three days more no appearance of disease remained; and under the use of aromatics and small doses of opium, he soon recovered his strength.

Case XLII

July 7th. Miss H—, of T—, Aet. 39. In the last state of phthisis pulmonalis became dropsical. She took the *Digitalis* without being relieved.

Case XLIII

July 9th. Mrs. F—, Aet. 70. A chearful, strong, healthy woman; but for a few years back had experienced a degree of difficult breathing when in exercise. In the course of the last year her legs swelled, and she felt great fulness about her stomach. These symptoms continued increasing very fast, notwithstanding several attempts made by a very judicious apothecary to relieve her. The more regular practitioner failing, she had recourse to a quack, who I believe plied her very powerfully with *Daphne laureola*, or some drastic purge of that kind. I found her greatly reduced in strength, her belly and lower extremities swollen to an amazing size, her urine small in quantity, and her appetite greatly impaired. For the first fortnight of my attendance blisters were applied, solution of fixed alkaly, decoction of *seneka* with vitriolic aether, (p. 41) chrystals of tartar, squill and cordial medicines were successively exhibited, but with no advantage. I then directed *Pulv. Fol. Digital.* two grains every four hours. After taking eighteen grains, the urine began to increase. The medicine was then stopped. The discharge of urine continued to increase, and in five or six days the whole of the dropsical water passed off, without any disturbance to the stomach or bowels. As the distension of the belly had been very great, a swathe was applied, and drawn gradually tighter as the water was evacuated. As no pains were spared to prevent the return of the dropsy, and as the best means I could devise proved unequal to my wishes, both in this and in some other cases, I shall take the liberty to point out the methods I tried at different times in as concise a manner as possible, for the knowledge of what will not do, may sometimes assist us to discover what will.

1780.

July 18th. Infusum amarum, stell, Seltzer water.

September 22d. Neutral saline draughts, with tinct. canthar.

26th. Pills of soap, garlic and millepedes.

30th. The same pills, with infusum amarum.

October 11th. Pills of aloes, assafetida, and sal martis, in the day-time, and mercury rubbed down, at night.

December 21st. The accumulation of water now required a repeti-

tion of the *Digitalis*. It was directed in infusion, a dram and half to eight ounces, and an ounce and half given every fourth hour, (p. 42) until its effects began to appear. The water was soon carried off.

30th. Sal diuretic. twice a day. To eat preserved garlic frequently.

1781.

February 1st. Pills of calomel, squill and gum ammoniac.

3d. Infusion of *Digitalis* repeated, and after the water was carried off, Dover's powder was tried as a sudorific.

March 18th. Infus. *Digitalis*. repeated.

26th. Pills of sal martis and aromatic species, with infusum amarum.

May 5th. Being feverish; James's powder and saline draughts.

10th. Laudanum every night, and an opening tincture to obviate costiveness.

24th. Infus. *Digitalis*, one ounce only every fourth hour, which soon procured a perfect evacuation of the water.

August 11th. Infus. *Digitalis*.

October 19th. An emetic, and fol. *Cicut.* pulv. ten grains every six hours.

November 8th. A mercurial bolus at bed-time.

16th. Infus. *Digitalis*.

December 23d. An emetic—Pills of seneka and gum ammoniac—Vitriolic acid in every thing she drinks.

25th. Squill united to small doses of opium.

1782.

January 2d. A troublesome cough—Syrup of garlic and oxymel of squills. A blister to the back.

4th. Tincture of cantharides and paregoric elixir. (p. 43)

28th. Infus. *Digitalis*, half an ounce every morning, and one ounce every night, was now sufficient to empty her.

March 26th. Infus. *Digitalis*; and when emptied, vitriol of copper twice a day.

April 1st. A cordial mixture for occasional use.

Two months afterwards a purging came on, which every now and then returned, inducing great weakness—her appetite failed, and she died in *July*.

Intervals

From *July* 9th, 1780, to *December* 21st, 171 days.

From *December* 21st to *February* 3d, 1781, 34 days.

From *February* 3d to *March* 18th, 44 days.

From *March* 18th to *May* 24th, 66 days.

From *May* 24th to *August* 11th, 79 days.

From *August* 11th to *November* 16th, 98 days.

From *November* 16th to *January* 28th, 1782, 74 days.

From *January* 28th to *March* 26th, 57 days.

None of the accumulations of water were at all equal to that which existed when I first saw her, for finding so easy a mode of relief, she became impatient under a small degree of pressure, and often insisted upon taking her medicine sooner than I thought it necessary. After the 26th of *March* the degree of effusion was inconsiderable, and at the time of her death very trifling, being probably carried off by the diarrhoea. (p. 44)

Case XLIV

July 12th. Mr. H——, of A——, Aet. 60. In the last stage of a life hurried to a termination by free living, dropsical symptoms became the most distressing. He wished to take the Digitalis. It was given, but afforded no relief.

Case XLV

July 13th. Mr. S——, Aet. 49. Asthma, or rather hydrothorax, anasarca, and symptoms of a diseased liver. He was directed to take two grains of Pulv. fol. Digital. every two hours, until it produced some effect. It soon removed the dropsical and asthmatic affections, and steel, with Seltzer water, restored him to health.

Case XLVI

August 6th. Mr. L——, Aet. 35. Ascites and anasarca. Pulv. Digital. grains three, repeated every fourth hour, until he had taken two scruples, removed every appearance of dropsy in a few days. He was then directed to take solution of merc. sublimat. and soon recovered his health and strength.

Case XLVII

August 16th. Mr. G——, of W——, Aet. 86. Asthma of many years duration, and lately an incipient anasarca, with a paucity of urine. He had never lived intemperately, was of a chearful disposition, and very sensible: for some years back had (p. 45) lost all relish for animal food, and his only support had been an ounce or two of bread and cheese, or a small slice of seed-cake, with three or four pints of mild ale, in the twenty-four hours. After trying chrystals of tartar, fixed alkaly, squills, &c. I directed three grains of Pulv. fol. Digital. made into pills, with G. ammoniac, to be given every six hours; this presently occasioned copious discharges of urine, removed his swellings, and restored him to his usual standard of health.

Case XLVIII

August 17th. T—— B——, Esq. of K——, Aet. 46. Jaundice, dropsy, and great hardness in the region of the liver. Infusion of Digitalis carried off all the effusion, and afterwards a course of deobstruent and tonic medicines removed his other complaints.

Case XLIX

August 23d. Mr. C——, Aet. 58. (The person mentioned at Case XXIII.) He had continued free from dropsy until within the last six weeks, his appetite was now totally gone, his strength extremely reduced, and the yellow of his jaundice changed to a blackish hue. The Digitalis was now tried in vain, and he died shortly afterwards.

Case L

August 24th. Mrs. W——, Aet. 39. Anasarcous legs and symptoms of hydrothorax, consequent (p. 46) to a tertian ague. Three grains of Pulv. Digitalis, given every fourth hour, occasioned a very copious flow of urine, and she got well without any other medicine.

Case LI

August 28th. Mr. J—— H——, Aet. 27. In consequence of very free living, had an ascites and swelled legs. I ordered him to take two grains of Fol. Digital. pulv. every two hours, until it produced some effect; a few doses caused a plentiful secretion of urine, but no sickness, or purging: in six days the swellings disappeared, and he has since remained in good health.

Case LII

September 27th. Mr. S——, Aet. 45. Had been long in an ill state of health, from what had been supposed an irregular gout, was greatly emaciated, had a sallow complexion, no appetite, costive bowels, quick and feeble pulse. The cause of his complaints was involved in obscurity; but I suspected the poison of lead, and was strengthened in this suspicion, upon finding his wife had likewise ill health, and, at times, severe attacks of colic; but the answers to my enquiries seemed to prove my suspicions fruitless, and, amongst other things, I was told the pump was of wood. He had lately suffered extremely from difficult breathing, which I thought owing to anasarcaous lungs; there was also a slight degree of pale swelling in his legs. Pulv. (p. 47) fol. Digital. made into pills, with gum ammoniac and aromatic species, soon relieved his breathing. Attempts were then made to assist him in other respects, but with little good effect, and some months afterwards he died, with every appearance of a worn out constitution.

About two years after this gentleman's death, I was talking to a pump-maker, who, in the course of conversation, mentioned the corrosion of leaden pumps, by some of the water in this town, and instanced that at the house of Mr. S——, which he had replaced with a wooden one about three years before. The lead, he said, was eaten away, so as to be very thin in some places, and full of holes in others;—this accidental information explained the mystery.

The deleterious effects of lead seem to be considerably modified by the constitution of the patient; for in some families only one or two individuals shall suffer from it, whilst the rest receive it with impunity. In the spring of the year 1776, I was desired

to visit Mrs. H——, of S—— Park, who had repeatedly been attacked with painful colics, and had suffered much from insuperable costiveness; I suspected lead to be the cause of her complaints, but was unable to trace by what means it was taken. She was relieved by the usual methods; but, a few months afterwards, I was desired to see her again: her sufferings were the same as before, and notwithstanding every precaution to guard against costiveness, she was never in perfect health, and seldom (p. 48) escaped severe attacks twice or thrice in a year; she had also frequent pains in her joints. I could not find any traces of similar complaints either in Mr. H——, the children, or the servants. Mrs. H—— was a water drinker, and seldom tasted any fermented liquor. The pump was of wood, as I had been informed upon my first visit. Her health continued nearly in the same state for two or three years more, but she always found herself better if she left her own house for any length of time. At length it occurred to me, that though the pump was a wooden one, the piston might work in lead. I therefore ordered the pump rods to be drawn up, and upon examination with a magnifying glass, found the leather of the piston covered with an infinite number of very minute shining particles of lead. Perhaps in this instance the metal was so minutely divided by abrasion, as to be mechanically suspended in the water. The lady was directed to drink the water of a spring, and never to swallow that from the pump. The event confirmed my suspicions, for she gradually recovered a good state of health, lost the obstinate costiveness, and has never to this day had any attack of the colic.

Case LIII

September 28th. Mrs. J——, Aet. 70. Ascites and very thick anasarcaous legs and thighs, total loss of strength and appetite. Infusion of Digitalis was given, but, as had been prognosticated, with no good effect.

(p. 49) Case LIV

September 30th. Mr. A——, Aet. 57. A strong man; hydrothorax and swelled legs; in other respects not unhealthful. He was directed to take two grains of the Pulv. fol. Digit. made into

a pill with gum ammoniac. Forty grains thus taken at intervals, effected a cure by increasing the quantity of urine, and he has had no relapse.

Case LV

November 2d. Mr. P——, of T——, Aet. 42. A very strong man, drank a great quantity of strong ale, and was much exposed to alterations of heat and cold. About the end of summer found himself short winded, and lost his appetite. The dyspnoea gradually increased, he got a most distressing sense of tightness across his stomach, his urine was little, and high coloured, and his legs began to swell; his pulse slender and feeble. From the 20th of *September* I frequently saw him, and observed a gradual and regular increase of all his complaints, notwithstanding the use of the most powerful medicines I could prescribe. He took chrystals of tartar, seneka, gum ammoniac, saline draughts, emetics, tinct. of cantharides, spirits of nitre dulcified, squills in all forms, volatile alkaly, calomel, Dover's powder, &c. Blisters and drastic purgatives were tried, interposing salt of steel and gentian. I had all along felt a reluctance to prescribe the *Digitalis* in this case, from a persuasion that it would not succeed. (p. 50) At length I was compelled to it, and directed one grain to be given every two hours until it should excite nausea. This it did; but, as I expected, it did no more. The reason of this belief will be mentioned hereafter. Five days after this last trial I gave him *assafetida* in large quantity, flattered by a hope that his extreme sufferings from the state of his respiration, might perhaps arise in part from spasm, but my hopes were in vain. I now thought of using an infusion of tobacco, and prescribed the following:

R. Fol. Nicotian. incis. drams ii.

Aq. bull. lb. ss.

Sp. Vini rectific. oz. i digere per horam.

I directed a spoonful of this to be given every two hours until it should vomit. This medicine had no better effect than the former ones, and he died some days afterwards.

Case LVI

November 6th. Mr. H—, Aet. 47. In the last state of phthisis pulmonalis, suffered much from dyspnoea, and anasarca. Squill medicines gave no relief. Digitalis in pills, with gum ammon, purged him, but opium being added, that effect ceased, and he continued to be relieved by them as long as he lived.

(p. 51) Case LVII

November 16th. Mrs. F—, Aet. 53. In *August* last was suddenly seized with epileptic fits, which continued to recur at uncertain intervals. Her belly had long been larger than natural, but without any perceptible fluctuation. Her legs and thighs swelled very considerably the beginning of this month, and now there was evidently water in the abdomen. The medicines hitherto in vain directed against the epileptic attacks, were now suspended, and two grains of the Pulv. fol. Digital, directed to be taken every six hours. The effects were most favourable, and the dropsical symptoms were soon removed by copious urinary discharges.

The attacks of epilepsy ceased soon afterwards. In *February*, 1781, there was some return of the swellings, which were soon removed, and she now enjoys very good health. Does not the narrative of this case throw light upon the nature of the epilepsy which sometimes attacks women, soon after the cessation of the menstrual flux?

1781

Case LVIII

January 1st. Mrs. G—, of H—, Aet. 62. Ascites and very large hard legs. After trying various medicines, under the direction of a very able physician, I ordered her to take one grain of Pulv. (p. 52) Digital. every six hours, but it produced no effect. Other Medicines were then tried to as little purpose. About the end of *February*, I directed an infusion of the Fol. Digital. but with no better success. Other methods were thought of, but none proved efficacious, and she died a few weeks afterwards.

Case LIX

January 3d. Mrs. B——, Aet. 53. Ascites, anasarca, and jaundice. After a purge of calomel and jallap, was ordered the Infusion of Digitalis: it acted kindly as a diuretic, and greatly reduced her swellings. Other medicines were then administered, with a view to her other complaints, but to no purpose, and she died about a month afterwards.

Case LX

January 14th. Mr. B——, of D——. Jaundice and ascites, the consequences of great intemperance. Extremely emaciated; his tongue and fauces covered with aphthous crusts, and his appetite gone. He first took tincture of cantharides with infusum amarum, then vitriolic salts, and various other medicines without relief; Infusum Digitalis was given afterwards, but was equally unsuccessful.

Case LXI

February 2d. I was desired by the late learned and ingenious Dr. Groome, to visit Miss S——, a (p. 53) young lady in the last state of emaciation from a dropsy. Every probable means to relieve her had been attempted by Dr. Groome, but to no purpose; and she had undergone the operation of the paracentesis repeatedly. The Doctor knew, he said, that I had cured many cases of dropsy, by the Digitalis, after the other more usual methods had been attempted without success, and he wished this lady to try that medicine under my direction; after examining the patient, and enquiring into the history of the disease, I was satisfied that the dropsy was encysted, and that no medicine could avail. The Digitalis, however, was directed, and she took it, but without advantage. She had determined not to be tapped again, and neither persuasion, nor distress from the distension, could prevail upon her: I at length proposed to make an opening into the sac, by means of a caustic, which was done under the judicious management of Mr. Wainwright, surgeon, at Dudley. The water was evacuated without any accident, and the patient

afterwards let it out herself from time to time as the pressure of it became troublesome, until she died at length perfectly exhausted.

Query. Is there not a probability that this method, assisted by bandage, might be used so as to effect a cure, in the earlier stages of ovarium dropsy?

Case LXII

February 27th. Mrs. O—, of T—, Aet. 52, with a constitution worn out by various complicated (p. 54) disorders, at length became dropsical. The Digitalis was given in small doses, in hopes of temporary benefit, and it did not fail to fulfil our expectations.

Case LXIII

March 16th. Mrs. P—, Aet. 47. Great debility, pale countenance, loss of appetite, legs swelled, urine of small quantity. A dram of Fol. siccat. Digital. in a half pint infusion was ordered, and an ounce of this infusion directed to be taken every morning. Myrrh and steel were given at intervals. Her urine soon increased, and the symptoms of dropsy disappeared.

Case LXIV

March 18th. Mr. W—, in the last stage of a pulmonary consumption became dropsical. The Digitalis was given, but without any good effect.

Case LXV

April 6th. Mr. B—, Aet. 63. For some years back had complained of being asthmatical, and was not without suspicion of diseased viscera. The last winter he had been mostly confined to his house, became dropsical, lost his appetite, and his skin and eyes turned yellow. By the use of medicines of the deobstruent class he became less discoloured, and the hardness about his stomach seemed to yield; but the ascites and anasarca symptoms increased so as to oppress his breathing (p. 55) exceedingly. Alkaline salts, and other diuretics failing of their effects, I ordered him to take an infus. of Digitalis. It operated so powerfully that it became necessary to support him with cordials

and blisters, but it freed him from the dropsy, and his breath became quite easy. He then took soap, rhubarb, tartar of vitriol, and steel, and gradually attained a good state of health, which he still continues to enjoy.

Case LXVI

April 8th. Mr. B—, Aet. 60. A corpulent man, with a stone in his bladder, from which at times his sufferings are extreme. He had been affected with what was supposed to be an asthma, for several years by fits, but through the last winter his breath had been much worse than usual; universal anasarca came on, and soon afterwards an ascites. Now his urine was small and much saturated, the dysuria was more dreadful than ever; his breath would not allow him to lie in bed, nor would the dysuria permit him to sleep; in this distressful situation, after having used other medicines to little purpose, I directed an infusion of *Digitalis* to be given. When the quantity of urine became more plentiful, the pain from his stone grew easier; in a few days the dropsy and asthma disappeared, and he soon regained his usual strength and health. Every year since, there has been a tendency to a return of these complaints, but he has recourse to the infusion, and immediately removes them.

(p. 56) *Case LXVII*

April 24th. Mr. M—, of C—, Aet. 57. Asthma, anasarca, jaundice, and great hardness and straitness across the region of the stomach. After a free exhibition of neutral draughts, alkaline salt, &c. the dropsy and difficult breathing remaining the same, he took *Infusum Digitalis*, which removed those complaints. He never lost the hardness about his stomach, but enjoyed very tolerable health for three years afterwards, without any return of the dropsy.

Case LXVIII

April 25th. Mrs. J—, Aet. 42. Phthisis pulmonalis and anasarcous legs and thighs. She took the *Infusum Digitalis* without effect. Myrrh and steel, with fixed alkaly, were then ordered, but to no purpose.

Case LXIX

May 1st. Master W——, of St. —, Aet. 6. I found him with every symptom of hydrocephalus internus. As it was yet early in the disease, in consequence of ideas which will be mentioned hereafter, I directed six ounces of blood to be immediately taken from the arm; the temporal artery to be opened the succeeding day; the head to be shaven, and six pints of cold water to be poured upon it every fourth hour, and two scruples of strong mercurial (p. 57) ointment to be rubbed into the legs every day. Five days afterwards, finding the febrile symptoms very much abated, and judging the remaining disease to be the effect of effusion, I directed a scruple of *Fol. Digital. sicc.* to be infused in three ounces of water, and a tablespoonful of the infusion to be given every third or fourth hour, until its action should be somewhat sensible. The effect was, an increased secretion of urine; and the patient soon recovered.

Case LXX

May 3d. Mrs. B——, Aet. 59. Ascites and anasarca, with strong symptoms of diseased viscera. *Infusum Digitalis* was at first prescribed, and presently removed the dropsy. She was then put upon saline draughts and calomel. After some time she became feverish: the fever proved intermittent, and was cured by the bark.

Case LXXI

May 3d. Mr. S——, Aet. 48. A strong man, who had lived intemperately. For some time past his breath had been very short, his legs swollen towards evening, and his urine small in quantity. Eight ounces of the *Infus. Digitalis* caused a considerable flow of urine; his complaints gradually vanished, and did not return.

(p. 58) Case LXXII

May 24th. Joseph B——, Aet. 50. Ascites, anasarca, and jaundice, from intemperate living. Infusion of *Digitalis* produced nausea, and lowered the frequency of the pulse; but had

no other sensible effects. His disorder continued to increase, and killed him about two months afterwards.

Case LXXIII

June 29th. Mr. B——, Aet. 60. A hard drinker; afflicted with asthma, jaundice, and dropsy. His appetite gone; his water foul and in small quantity. Neutral saline mixture, chrysalts of tartar, vinum chalybeat. and other medicines had been prescribed to little advantage. Infusion of *Fol. Digitalis* acted powerfully as a diuretic, and removed the most urgent of his complaints, viz. the dropsical and asthmatical symptoms.

The following winter his breathing grew bad again, his appetite totally failed, and he died, but without any return of the ascites.

Case LXXIV

June 29th. Mr. A——, Aet. 58. Kept a public house and drank very hard. He had symptoms of diseased viscera, jaundice, ascites, and anasarca. After taking various deobstruents and diuretics, to no purpose, he was ordered the Infusion of *Digitalis*: (p. 59) a few doses occasioned a plentiful flow of urine, relieved his breath, and reduced his swellings; but, on account of his great weakness, it was judged imprudent to urge the medicine to the entire evacuation of the water. He was so much relieved as to be able to come down stairs and to walk about, but his want of appetite and jaundice continuing, and his debility increasing, he died in about two months.

Case LXXV

July 18th. Mrs. B——, Aet. 46. A little woman, and very much deformed. Asthmatical for many years. For several months past had been worse than usual; appetite totally gone, legs swollen, sense of great fulness about her stomach, countenance fallen, lips livid, could not lie down.

The usual modes of practice failing, the *Digitalis* was tried, but with no better success, and in about a month she died; not without suspicion of her death having been accelerated a few

days, by her taking half a grain of opium. This may be a caution to young practitioners to be careful how they venture upon even small doses of opium in such constitutions, however much they may be urged by the patient to prescribe something that may procure a little rest and ease.

(p. 60) *Case LXXVI*

August 12th. Mr. L——, Aet. 65, the person whose Case is recorded at No. XXIV, had a return of his insanity, after near two years perfect health. He was extremely reduced when I saw him, and the medicine which cured him before was now administered without effect, for his weakness was such that I did not dare to urge it.

Case LXXVII

September 10th. Mr. V——, of S——, Aet. 47. A man of strong fibre, and the remains of a florid complexion. His disease an ascites and swelled legs, the consequence of a very free course of life; he had been once tapped, and taken much medicine before I saw him. The Digitalis was now directed; it lowered his pulse, but did not prove diuretic. He returned home, and soon after was tapped again, but survived the operation only a few hours.

Case LXXVIII

September 25th. Mr. O——, of M——, Aet. 63. Very painful and general swellings in all his limbs, which had confined him mostly to his bed since the preceding winter; the swellings were uniform, tense, and resisting, but the skin not discoloured. After trying guiacum and Dover's powder without advantage, I directed Infusion of Digitalis. It acted on the kidneys, but did not relieve him. It is not (p. 61) easy to say what the disease was, and the patient living at a distance, I never learnt the future progress or termination of it.

Case LXXIX

September 26th. Mr. D——, Aet. 42, a very sensible and judicious surgeon at B——, in Staffordshire, laboured under ascites

and very large anasarca legs, together with indubitable symptoms of diseased viscera. Having tried the usual diuretics to no purpose, I directed a scruple of Fol. Digital. sicat. in a four ounce infusion, a table spoonful to be taken twice a day. The second bottle wholly removed his dropsy, which never returned.

Case LXXX

September 27th. Mrs. E—, Aet. 42. A fat sedentary woman; after a long illness, very indistinctly marked; had symptoms of enlarged liver and dropsy. In this case I was happy in the assistance of Dr. Ash. Digitalis was once exhibited in small doses, but to no better purpose than many other medicines. She suffered great pain in the abdomen for several weeks, and after her death, the liver, spleen, and kidneys were found of a pale colour, and very greatly enlarged, but the quantity of effused fluid in the cavity was not more than a pint.

(p. 62) Case LXXXI

October 28th. Mr. B—, Aet. 33. Had drank an immense quantity of mild ale, and was now become dropsical. He was a lusty man, of a pale complexion: his belly large, and his legs and thighs swollen to an enormous size. I directed the Infusion of Digitalis, which in ten days completely emptied him. He was then put upon the use of steel and bitters, and directed to live temperately, which I believe he did, for I saw him two years afterwards in perfect health.

Case LXXXII

November 14th. Mr. W—, of T—, Aet. 49. A lusty man, with an asthma and anasarca. He had taken several medicines by the direction of a very judicious apothecary, but not getting relief as he had been accustomed to do in former years, he came under my direction. For the space of a month I tried to relieve him by fixed alkaly, seneka, Dover's powder, gum ammoniac, squill, &c. but without effect. I then directed Infusion of Digitalis, which soon increased the flow of urine without exciting nausea, and in a few days removed all his complaints.

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Case LXXXIII

January 23d. Mr. Q——, Aet. 74. A stone in his bladder for many years; dropsical for the last three months. Had taken at different times soap with squill and gum ammoniac; soap lees; chrystals of tartar, oil of juniper, seneka, jallap, &c. but the dropsical symptoms still increased, and the dysuria from the stone became very urgent. I now directed a dram of the Fol. Digit. sicc. in a half pint infusion, half an ounce to be given every six hours. This presently relieved the dysuria, and soon removed the dropsy, without any disturbance to his system.

Case LXXXIV

January 27th. Mr. D——, Aet. 86. The debility of age and dropsical legs had long oppressed him. A few weeks before his death his breathing became very short, he could not lie down in bed, and his urine was small in quantity. A wine glass of a weak Infusion of Digitalis, warmed with aromatics, was ordered to be taken twice a day. It afforded a temporary relief, but he did not long survive.

Case LXXXV

January 28th. Mr. D——, Aet. 35. A publican and a hard drinker. Ascites, anasarca, diseased (p. 64) viscera, and slight attacks of haemoptoe. A dram of Fol. Digital. sicc. in a half pint infusion, of which one ounce was given night and morning, proved diuretic and removed his dropsy. He then took medicines calculated to relieve his other complaints. The dropsy did not return during my attendance upon him, which was three or four weeks. A quack then undertook to cure him with blue vitriol vomits, but as I am informed, he presently sunk under that rough treatment.

Case LXXXVI

January 29th. Mrs. O——, of D——, Aet. 53. A constant and distressing palpitation of her heart, with great debility.

From a degree of anasarca in her legs I was led to suspect effusion in the Pericardium, and therefore directed Digitalis, but it produced no benefit. She then took various other medicines with the same want of success, and about ten months afterwards died suddenly.

Case LXXXVII

January 31st. Mr. T—, of A—, Aet. 81. Great difficulty of breathing, so that he had not lain in bed for the last six weeks, and some swelling in his legs. These complaints were subsequent to a very severe cold, and he had still a troublesome cough. He told me that at his age he did not look for a cure, but should be glad of relief, if it could be obtained without taking much medicine. I directed an Infusion of Digitalis, a dram to eight ounces, (p. 65) one spoonful to be taken every morning, and two at night. He only took this quantity; for in four days he could lie down, and soon afterwards quitted his chamber. In a month he had a return of his complaints, and was relieved as before.

Case LXXXVIII

January 31st. Mrs. J—, of S—, Aet. 67. A lusty woman, of a florid complexion, large belly, and very thick legs. She had been kept alive for some years by the discharge from ulcers in her legs; but the sores now put on a very disagreeable livid appearance, her belly grew still larger, her breath short, her pulse feeble, and she could not take nourishment. Several medicines having been given in vain, the Digitalis was tried, but with no better effect; and in about a month she died.

Case LXXXIX

February 2d. Mr. B—, Aet. 73. An universal dropsy. He took various medicines, and Digitalis in small doses, but without any good effect.

Case XC

February 24th. Master M—, of W—, Aet. 10. An epilepsy of some years continuance, which had never been interrupted by any of the various methods tried for his relief. The

Digitalis was given for a few days, but as he lived at a distance, so that I could not attend to its effects, he only took one (p. 66) half pint infusion, which made no alteration in his complaint.

Case XCI

March 6th. Mr. H—, Aet. 62. A very hard drinker, and had twice had attacks of apoplexy. He had now an ascites, was anasarcaous, and had every appearance of a diseased liver. Small doses of calomel, Dover's powder, infusum amarum, and sal sodae palliated his symptoms for a while; these failing; blisters, squills, and cordials were given without effect. A weak Infusion of Digitalis, well aromatised, was then directed to be given in small doses. It rather seemed to check than to increase the secretion of urine, and soon produced sickness. Failing in its usual effect, the medicine was no longer continued; but every thing that was tried proved equally inefficacious, and he did not long survive.

Case XCII

May 10th. Mrs. P—, Aet. 40. Spasmodic asthma of many years continuance, which had frequently been relieved by ammoniacum, squills, &c. but these now failing in their wonted effects, an Infus. of Fol. Digitalis was tried, but it seemed rather to increase than relieve her symptoms.

Case XCIII

May 22d. Mr. O—, of B—, Aet. 61. A very large man, and a free liver; after an attack of (p. 67) hemiplegia early in the spring, from which he only partially recovered, became dropsical. The dropsy occupied both legs and thighs, and the arm of the affected side. I directed an Infusion of Digitalis in small doses, so as not to affect his stomach. The swellings gradually subsided, and in the course of the summer he recovered perfectly from the palsy.

Case XCIV

July 5th. Mr. C—, of W—, Aet. 28. Had drank very freely both of ale and spirits; and in consequence had an ascites,

very large legs, and great fulness about the stomach. He was ordered to take the Infusion of Digitalis night and morning for a few days, and then to keep his bowels open with chrystals of tartar. The first half pint of infusion relieved him greatly; after an interval of a fortnight it was repeated, and he got well without any other medicine, only continuing the chrystals of tartar occasionally. I forgot to mention that this gentleman, before I saw him, had been for two months under the care of a very celebrated physician, by whose direction he had taken mercurials, bitters, squills, alkaline salts, and other things, but without much advantage.

Case XCV

March 6th. Mrs. W—, Aet. 36. In the last stage of a pulmonary consumption, took the Infus. Digitalis, but without any advantage.

(p. 68) *Case XCVI*

August 20th. Mr. P—, Aet. 43. In the year 1781 he had a severe peripneumony, from which he recovered with difficulty. At the date of this, when he first consulted me, the symptoms of hydro-thorax were pretty obvious. I directed a purge, and then the Infusum Digitalis, three drams to half a pint, one ounce to be taken every four hours. It made him sick, and occasioned a copious discharge of urine. His complaints immediately vanished, and he remains in perfect health.

Case CVII

September 24th. Mrs. R—, of B—, Aet. 35, the mother of many children. After her last lying in, three months ago, had that kind of swelling in one of her legs which is mentioned at No. VIII, XXVI, and XXXI. A considerable degree of swelling still remained; the limb was heavy to her feeling, and not devoid of pain. I directed a bolus of five grains of Pulv Digitalis, and twenty-five of crude quicksilver rubbed down, with conserve of cynosbat. to be taken at bed-time, and after-

wards an Infusion of red bark and Fol. Digitalis to be taken twice a day. There was half an ounce of bark and half a dram of the leaves in a pint infusion: the dose two ounces.

The leg soon began to mend, and two pints of the infusion finished the cure.

(p. 69) *Case XCVIII*

September 25th. Mr. R——, Aet. 60. Complained to me of a sickness after eating, and for some weeks past he had thrown up all his food, soon after he had swallowed it. He had taken various medicines, but found benefit from none, and had tried various kinds of diet. He was now very thin and weak, but had a good appetite. As several very probable methods had been prescribed, and as the usual symptoms of organic disease were absent, I determined to give him a spoonful of the Infusion of Digitalis twice a day; made by digesting two drams of the dried leaves in half a pint of cinnamon water. From the time he began to take this medicine he suffered no return of his complaint, and soon recovered his flesh and his strength.

It should be observed, that I had frequently seen the Digitalis remove sickness, though prescribed for very different complaints.

Case XCIX

September 30th. Mrs. A——, Aet. 38. Hydro-thorax and anasarca. Her chest was very considerably deformed. One half pint of the Digitalis Infusion entirely cured her.

(p. 70) *Case C*

September 30th. Mr. R——, of W——, Aet. 47. Hydro-thorax and anasarca. An Infusion of Digitalis was directed, and after the expected effects from that should take place, sixty drops of tincture of cantharides twice a day. As he was costive pills of aloes and steel were ordered to be taken occasionally.

This plan succeeded perfectly. About a month afterwards he had some rheumatic affections, which were removed by guiacum.

Case CI

October 2d. Mrs. R—, Aet. 60. Diseased viscera; ascites and anasarca. Had taken various deobstruent and diuretic medicines to little purpose. The *Digitalis* brought on a nausea and languor, but had no effect on the kidneys.

Case CII

October 12th. Mr. R—, Aet. 41. A publican, and a hard drinker. His legs and belly greatly swollen; appetite gone, countenance yellow, breath very short, and cough troublesome. After a vomit I gave him calomel, saline draughts, steel and bitters, &c. He had taken the more usual diuretics before I saw him. As the dropsical symptoms increased, I changed his medicines for pills made of (p. 71) soap, containing two grains of *Pulv. fol. Digital.* in each dose, and, as he was costive, two grains of jallap. He took them twice a day, and in a week was free from every appearance of dropsy. The jaundice soon afterwards vanished, and tonics restored him to perfect health.

Case CIII

October 12th. Mr. B—, Aet. 39. Kept a public house, drank very freely, and became dropsical; he complained also of rheumatic pains. I directed Infusion of *Digitalis*, half an ounce twice a day. In eight days the swellings in his legs and the fullness about his stomach disappeared. His rheumatic affections were cured by the usual methods.

Case CIV

October 22d. Master B—, Aet. 3. Ascites and universal anasarca. Half a grain of *Fol. Digital. sicc.* given every six hours, produced no effect; probably the medicine was wasted in giving. An infusion of the dried leaf was then tried, a dram to four ounces, two tea spoonfuls for a dose; this soon increased the flow of urine to a very great degree, and he got perfectly well.

Case CV

October 30th. Mr. G——, of W——, Aet. 88. The gentleman mentioned in No. XLVII. His complaints and manner of living the same as there (p. 72) mentioned. I ordered an Infusion of the Digitalis, a dram and half to half a pint; one ounce to be taken twice a day; which cured him in a short time.

On *March* the 23d, 1784, he sent for me again. His complaints were the same, but he was much more feeble. On this account I directed a dram of the Fol. Digitalis to be infused for a night in four ounces of spirituous cinnamon water, a spoonful to be taken every night. This had not a sufficient effect; therefore, on the 22d of *April*, I ordered the infusion prescribed two years before, which soon removed his complaints.

He died soon afterwards, fairly worn out, in his ninetieth year.

Case CVI

November 2d. Mr. S——, of B——h——, Aet. 61. Hydrothorax and swelled legs. Squills were given for a week in very full doses, and other modes of relief attempted; but his breathing became so bad, his countenance so livid, his pulse so feeble, and his extremities so cold, that I was apprehensive upon my second visit that he had not twenty-four hours to live. In this situation I gave him the Infusum Digitalis stronger than usual, viz. two drams to eight ounces. Finding himself relieved by this, he continued to take it, contrary to the directions given, after the diuretic effects had appeared.

(p. 73) The sickness which followed was truly alarming; it continued at intervals for many days, his pulse sunk down to forty in a minute, every object appeared green to his eyes, and between the exertions of reaching he lay in a state approaching to syncope. The strongest cordials, volatiles, and repeated blisters barely supported him. At length, however, he did begin to emerge out of the extreme danger into which his folly had plunged him; and by generous living and tonics, in about two months he came to enjoy a perfect state of health.

Case CVII

November 19th. Master S——, Aet. 8. Ascites and anasarca. A dram of Fol. Digitalis in a six ounce infusion, given in doses of a spoonful, effected a perfect cure, without producing nausea.

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The reader will perhaps remark, that from the middle of *January* to the first of *May*, not a single case occurs, and that the amount of cases is likewise less than in the preceding or ensuing years; to prevent erroneous conjectures or conclusions, it may be expedient to mention, that the ill state of my own health obliged me to retire from business for some time in the spring of the year, and that I did not perfectly recover until the following summer.

(p. 74) *Case CVIII*

January 15th. Mrs. G——, Aet. 57. A very fat woman; has been dropsical since *November* last; with symptoms of diseased viscera. Various remedies having been taken without effect, an Infusion of Digitalis was directed twice a day, with a view to palliate the more urgent symptoms. She took it four days without relief, and as her recovery seemed impossible it was urged no farther.

Case CIX

May 1st. Mrs. D——, Aet. 72. A thin woman, with very large anasarcous legs and thighs; no appetite and general debility. After a month's trial of cordials and diuretics of different kinds, the surgeon who had scarified her legs apprehended they would mortify; she had very great pain in them, they were very red and black by places, and extremely tense. It was evident that unless the tension could be removed, gangrene must soon ensue. I therefore gave her Infusum Digitalis, which increased the secretion of urine by the following evening, so that the great tension began to abate, and together with it the pain and inflammation. She was so feeble that I dared not urge the medicine further, but she occasionally took it at intervals until the time of her death, which happened a few weeks afterwards.

(p. 75) *Case CX*

May 18th. I was desired to prescribe for May Bowen, a poor girl at Hagley. Her disease appeared to me to be an ovarium dropsy. In other respects she was in perfect health. I directed the Digitalis to be given, and gradually pushed so as to affect her very considerably. It was done; but the patient still carries her big belly, and is otherwise very well.

Case CXI

May 25th. Mr. G——, Aet. 28. In the last stage of a pulmonary consumption of the scrophulous kind, took an Infusion of Digitalis, but without any advantage.

Case CXII

May 31st. Mr. H——, Aet. 27. In the last state of a phthisis pulmonalis became dropsical. He took half a pint of the Infusum Digitalis in six days, but without any sensible effect.

Case CXIII

June 3d. Master B——, of D——, Aet. 6. With an universal anasarca, had an extremely troublesome cough. An opiate was given to quiet the cough at night, and 2 tea spoonfuls of Infus. Digit. were ordered every six hours. The dropsy was presently removed; but the cough continued, his (p. 76) flesh wasted, his strength failed, and some weeks afterwards he died tabid.

Case CXIV

June 19th. Mrs. L——, Aet. 28. A dropsy in the last stage of a phthisis. Infusum Digitalis was tried to no purpose.

Case CXV

June 20th. Mrs. H——, Aet. 46. A very fat, short woman, had suffered severely through the last winter and spring from what had been called asthma; but for some time past an universal anasarca prevailed, and she had not lain down for several weeks. After trying vitriolic acid, tincture of cantharides, squills, etc.

without advantage, she took half a pint of Infus. Digitalis in three days. In a week afterwards the dropsical symptoms disappeared, her breath became easy, her appetite returned, and she recovered perfect health. The infusion neither occasioned sickness nor purging.

Case CXVI

June 24th. Mrs. B—, Aet. 40. A puerperal fever, and swelled legs and thighs. The fever not yielding to the usual practice, I directed an Infusion of Fol. Digitalis. It proved diuretic; the swellings subsided, but the fever continued, and a few days afterwards a diarrhoea coming on, she died.

(p. 77) *Case CXVII*

July 22d. Mr. F—, Aet. 48. A strong man, of a florid complexion, in consequence of intemperance became dropsical, with symptoms of diseased viscera, great dyspnoea, a very troublesome cough, and total loss of appetite. He took mild mercurials, pills of soap, rhubarb, and tartar of vitriol, with soluble tartar and dulcified spirits of nitre in barley water. After a reasonable trial of this plan; he took squill every six hours, and a solution of assafetida and gum ammoniac, to ease his breathing: finding no relief, I gave him chrystals of tartar with ginger; but his remaining health and strength daily declined, and he was not at all benefited by the medicines. I was averse to the use of Digitalis in this case, judging from what I had seen in similar instances of tense fibre, that it would not act as a diuretic. I therefore once more directed squill, with decoction of seneka and sal sodae; but it was inefficacious. His strength being much broken down, I then ordered gum ammoniac, with small doses of opium, and infusum amarum, continuing the squill at intervals. At length I was urged to give the Digitalis, and considering the case as desperate, I agreed to do it. The event was as I expected; no increase in the urine took place; and the medicine being still continued, his pulse became slow, and he apparently sunk under its sedative effects. He was neither purged nor vomited; and had the Digitalis either been omitted (p. 78) altogether, or sus-

pended upon its first effects upon the pulse being observed, he might perhaps have existed a week longer.

Case CXVIII

July 26th. Mr. W——, of W——, Aet. 47. Phthisis pulmonalis, jaundice, ascites, and swelled legs. As it was probable that the only relief I could give in a case so circumstanced, would be by carrying off the effused fluids. I tried squill and fixed alkaly; and these failing, I ordered the Infusum Digitalis. This had the desired effect, and, I believe, prolonged his life a few weeks.

Case CXIX

August 15th. Mrs. C——, Aet. 60. Ascites, anasarca, diseased viscera, paucity of urine, and total loss of appetite. These complaints had heretofore existed repeatedly, and had been removed by deobstruent and diuretic medicines; but in this attack the symptoms were suffered to exist a longer time and in a greater degree, before assistance was sought for. The remedies that used to relieve her were now exhibited to no purpose. Mild mercurials, soap, rhubarb, and squill were tried; but she grew rapidly worse. Saline draughts with acetum scilliticum seemed for a few days to check the progress of her complaint, but they soon lost their effect, and diarrhoea ensued upon every attempt to increase the frequency of the dose. Draughts with Infus. Digital. were then directed to be taken twice (p. 79) a day. The effect was a powerful action on the kidneys, and a reduction of the swellings, but without sickness. A degree of appetite returned, but still the tendency to diarrhoea existed, and kept her weak. Tonic medicines were then tried, but without advantage, and in a month it was necessary to have recourse to the Digitalis again. It was directed in a half pint mixture; an ounce to be taken thrice in twenty-four hours. On the 2d day, finding her symptoms very much relieved, she took in the absence of her nurse, nearly a double dose of the medicine. The consequence was great sickness, languor continuing for several days, and almost a total stop to the secretion of urine, from the time the sickness commenced.

without advantage, she took half a pint of Infus. Digitalis in three days. In a week afterwards the dropsical symptoms disappeared, her breath became easy, her appetite returned, and she recovered perfect health. The infusion neither occasioned sickness nor purging.

Case CXVI

June 24th. Mrs. B—, Aet. 40. A puerperal fever, and swelled legs and thighs. The fever not yielding to the usual practice, I directed an Infusion of Fol. Digitalis. It proved diuretic; the swellings subsided, but the fever continued, and a few days afterwards a diarrhoea coming on, she died.

(p. 77) *Case CXVII*

July 22d. Mr. F—, Aet. 48. A strong man, of a florid complexion, in consequence of intemperance became dropsical, with symptoms of diseased viscera, great dyspnoea, a very troublesome cough, and total loss of appetite. He took mild mercurials, pills of soap, rhubarb, and tartar of vitriol, with soluble tartar and dulcified spirits of nitre in barley water. After a reasonable trial of this plan, he took squill every six hours, and a solution of assafetida and gum ammoniac, to ease his breathing: finding no relief, I gave him chrystals of tartar with ginger; but his remaining health and strength daily declined, and he was not at all benefited by the medicines. I was averse to the use of Digitalis in this case, judging from what I had seen in similar instances of tense fibre, that it would not act as a diuretic. I therefore once more directed squill, with decoction of seneka and sal sodae; but it was inefficacious. His strength being much broken down, I then ordered gum ammoniac, with small doses of opium, and infusum amarum, continuing the squill at intervals. At length I was urged to give the Digitalis, and considering the case as desperate, I agreed to do it. The event was as I expected; no increase in the urine took place; and the medicine being still continued, his pulse became slow, and he apparently sunk under its sedative effects. He was neither purged nor vomited; and had the Digitalis either been omitted (p. 78) altogether, or sus-

pended upon its first effects upon the pulse being observed, he might perhaps have existed a week longer.

Case CXVIII

July 26th. Mr. W——, of W——, Aet. 47. Phthisis pulmonalis, jaundice, ascites, and swelled legs. As it was probable that the only relief I could give in a case so circumstanced, would be by carrying off the effused fluids. I tried squill and fixed alkaly; and these failing, I ordered the Infusum Digitalis. This had the desired effect, and, I believe, prolonged his life a few weeks.

Case CXIX

August 15th. Mrs. C——, Aet. 60. Ascites, anasarca, diseased viscera, paucity of urine, and total loss of appetite. These complaints had heretofore existed repeatedly, and had been removed by deobstruent and diuretic medicines; but in this attack the symptoms were suffered to exist a longer time and in a greater degree, before assistance was sought for. The remedies that used to relieve her were now exhibited to no purpose. Mild mercurials, soap, rhubarb, and squill were tried; but she grew rapidly worse. Saline draughts with acetum scilliticum seemed for a few days to check the progress of her complaint, but they soon lost their effect, and diarrhoea ensued upon every attempt to increase the frequency of the dose. Draughts with Infus. Digital. were then directed to be taken twice (p. 79) a day. The effect was a powerful action on the kidneys, and a reduction of the swellings, but without sickness. A degree of appetite returned, but still the tendency to diarrhoea existed, and kept her weak. Tonic medicines were then tried, but without advantage, and in a month it was necessary to have recourse to the Digitalis again. It was directed in a half pint mixture; an ounce to be taken thrice in twenty-four hours. On the 2d day, finding her symptoms very much relieved, she took in the absence of her nurse, nearly a double dose of the medicine. The consequence was great sickness, languor continuing for several days, and almost a total stop to the secretion of urine, from the time the sickness commenced.

The case now became totally unmanageable in my hands, and, after a fortnight, I was dismissed, and another physician called in: but she did not long survive.

This was not the first, nor the last instance, in which I have seen too large a *dose* of the medicine, defeat the very purpose for which it was directed.

Case CXX

August 22d. Mrs. S——, Aet. 36. Extreme faintiness; anasarous legs and thighs; great difficulty of breathing, troublesome cough, frequent chilly fits succeeded by hot ones; night sweats, and a tendency to diarrhoea. Apprehensive that the (p. 80) more urgent symptoms were caused by water in the lungs, I directed an Infusion of Digitalis, with an ounce of diacodium to the half pint to prevent it purging, a wine glass full to be taken every night at bed-time, and a mixture with confect. cardiac. and pulv. ipecac. to be given in small doses after every loose stool.

On the fourth day she was better in all respects; had made a large quantity of water and did not purge. In a few days more she lost all her complaints, except the cough, which gradually left her, without any further assistance.

I was agreeably deceived in the event of this case, for I expected after the water was removed, to have had a phthisis to contend with.

Case CXXI

August 25th. T—— W——, Esq; Aet. 50. A free liver, diseased viscera, belly very tense, and much swollen; fluctuation perceptible, but the swelling circumscribed; pulse 132. This gentleman was under the care of my very worthy friend Dr. Ash, who, having tried various modes of cure to no purpose, asked me if I thought the Digitalis would answer in this case. I replied that it would not, for I had never seen it effectual where the swelling appeared very tense and circumscribed. It was tried however, but did not lessen the swelling. I mention this case, to introduce the above remark, and also (p. 81) to point out the great effect the Digitalis has upon the action of the heart; for

the pulse came down to 96. He was afterwards tapped, and continued, for some time under our joint attendance, but the pulse never became quicker, nor did the swelling return.

Case CXXII

September 7th. Mr. L——, Aet. 43. After several severe attacks of ill formed gout, attended for some time past with jaundice and other symptoms of diseased viscera, the consequences of intemperate living, was sent to Buxton; from whence he returned in three weeks with ascites and anasarca. Under this complicated load of disease, I prescribed repeatedly without advantage, and at length gave him the Digitalis, which carried off the more obvious symptoms of dropsy; but the jaundice, loss of appetite, diseased viscera, &c. rendered his recovery impossible.

1784

Case CXXIII

February 12th. Mrs. C——, Aet. 54. A strong short woman of a florid complexion; complained of great fullness across the region of the stomach; short breath, a troublesome cough, loss of appetite, paucity of urine; and had a brownish yellow tinge on her skin and in her eyes. She dated these complaints from a fall she had through a trap door about the beginning of winter. From the beginning of January to this time, she had been repeatedly let (p. 82) blood, had taken calomel purges with jallap; pills of soap, rhubarb and calomel; saline julep with acet. scillit. nitrous decoction, garlic, mercury rubbed down, infus. amarum purg. &c. After the failure of medicines so powerful, and seemingly so well adapted, and during the use of which all the symptoms continued to increase, it was evident that a favourable event could not be expected. However, I tried the infusum Digitalis, but it did nothing. I then gave her pills of quicksilver, soap and squill, with decoction of dandelion, and after some time, chrystals of tartar with ginger. Nothing succeeded to our wishes, and the increase of orthopnoea compelled me occasionally to relieve her by drastic purges, but these diminished her strength,

more in proportion than they relieved her symptoms. Tincture of cantharides, sal diureticus and various other means were occasionally tried, but with very little effect, and she died towards the end of March.

Case CXXIV

March 31st. Miss W——, Aet. 60. Had been subject to peripneumonic affections in the winter. She had now total loss of appetite, very great debility, difficult breathing; much cough, a considerable degree of expectoration, and a paucity of urine. She had been blooded, taken soap, assaf. and squill, afterwards assaf. and ammon. with acet. scillit.: but all her complaints increasing, a blister was applied to her back, and the Digitalis infusion directed to be taken every night. The effect was an increased (p. 83) secretion of urine, a considerable relief to her breath and some return of appetite; but soon afterwards she became hectic, spat purulent matter, and died in a few weeks.

Case CXXV

April 12th. Mrs. H——, of L——, Aet. 61. In *December* last this Lady, then upon a visit in London, was attacked with severe symptoms of peripneumony. She was treated as an asthmatic patient, but finding no relief, she made an effort to return to her home to die. In her way through this place, the latter end of December, I was desired to see her. By repeated bleedings, blisters, and other usual methods, she was so far relieved, that she wished to remain under my care. After a while she began to spit matter and became hectic. With great difficulty she was kept alive during the discharge of the abscess, and about the end of March she had swelled legs, and unequivocal symptoms of dropsy in the chest. Other diuretics failing, on the 12th of April I was induced to give her the Digitalis in small doses. The relief was great and effectual. After an interval of fifteen days, some swellings still remaining in the legs, I repeated the medicine, and with such good effect, that she lost all her complaints, got a keen appetite, recovered her strength, and about the end of May undertook a journey of fifty miles to her own home, where she still remains in perfect health.

(p. 84) *Case CXXVI*

April 17th. Mr. F—, Aet. 59. A very fat man, and a free liver; had long been subject to what was called asthma, particularly in the winter. For some weeks past his legs swelled, he had great sense of fullness across his stomach; a severe cough; total loss of appetite, thirst great, urine sparing, his breath so difficult that he had not lain down in bed for several nights. Calomel, gum ammoniac, tincture of cantharides, &c. having been given in vain, I ordered two grains of pulv. fol. Digitalis made into pills, with aromatic species and syrup, to be given every night. On the third day his urine was less turbid; on the fourth considerably increased in quantity, and in ten days more he was free from all complaints, and has since had no relapse.

Case CXXVII

May 7th. Miss K—, Aet. 8. After a long continued ague, became hectic and dropsical. Her belly was very large, and she had a total loss of appetite. Half a grain of fol. Digital. pulv. with 2 gr. of merc. alcalis. were ordered night and morning, and an infusion of bark and rhubarb with steel wine to be given in the day time. Her belly began to subside in a few days, and she was soon restored to health. Two other children in the family, affected nearly in the same way, had died, from the parents being persuaded that an ague in the spring (p. 85) was healthful and should not be stopped.—I know not how far the recovery in this case may be attributed to the Digitalis, but the child was so near dying that I dared not trust to any less efficacious diuretic.

Case CXXVIII

June 13th. Mr. C—, Aet. 45. A fat man, had formerly drunk hard, but not latterly: last March began to complain of difficult breathing, swelled legs, full belly, but without fluctuation, great thirst, no appetite; urine thick and foul; complexion brownish yellow. Mercurial medicines, diuretics of different kinds, and bitters, had been trying for the last three months, but with little advantage. I directed two grains of the fol. Digital. in powder to be taken every night, and infus. amar. with tinct. sac. twice a day. In three days the quantity of his urine

increased, in ten or twelve days all his symptoms disappeared, and he has had no relapse.

Case CXXIX

June 17th. Mr. N—, of W—, Aet. 54. A large man, of a pale complexion; had been subject to severe fits of asthma for some years, but now worse than usual. The intermitting pulse, the great disturbance from change of posture, and the swelled legs induced me to conclude that the exacerbation of his old complaint was occasioned by serous effusion. I directed pills with a grain and half of the (p. 86) pulv. Digital. to be taken every night, and as he was costive, jallap made a part of the composition. He was also directed to take mustardseed every morning and a solution of assafetida twice in the day. The effect of this plan was perfectly to our wishes, and in a short time he recovered his usual health. About half a year afterwards he died apoplectic.

Case CXXX

Mary B—. A young unmarried woman. Her disease appeared to me a dropsy of the right ovary. She took an infusion of Digitalis, but, as I expected with no good effect. She is still, I am informed, nearly in the same state.

Case CXXXI

July 12th. Mrs. A—, of C—, Aet. 56. After a series of indispositions for several years, became dropsical; and had long been confined to her chamber, unable to lie down or to walk. She was so feeble, her legs so much swelled, her breath so short, and the symptoms of diseased viscera so strong, that I dared not to entertain hopes of a cure; but wishing to relieve her more urgent symptoms, directed quicksilver rubbed down and sol. Digital. pulv. to be made into pills: the dose, containing two grains of the latter, to be given night and morning. She was also ordered to take a draught with a dram of aether twice a day, and to have scapulary issues. Her breath was so much relieved, (p. 87) that she was able soon afterwards to come down

stairs; but her constitution was too much broken to admit of a recovery.

Case CXXXII

July 16th. Mr. B—, of W—, Aet. 31. After a tertian ague of 12 months continuation, suffered great indisposition for 10 months more. He chiefly complained of great straitness and pain in the hypochondriac region, very short breath, swelled legs, want of appetite. He had been under the care of some very sensible practitioners, but his complaints increased, and he determined to come to Birmingham. I found him supported upright in his chair, by pillows, every attempt to lean back or stoop forward giving him the sensation of instantaneous suffocation. He said he had not been in bed for many weeks. His countenance was sunk and pale; his lips livid; his belly, thighs and legs very greatly swollen; hands and feet cold, the nails almost black, pulse 160 tremulous beats in a minute, but the pulsation in the carotid arteries was such as to be visible to the eye, and to shake his head so that he could not hold it still. His thirst was very great, his urine small in quantity, and he was disposed to purge. I immediately ordered a spoonful of the infusum *Digitalis* every six hours, with a small quantity of laudanum, to prevent its running off by stool, and decoction of *leontodon taraxacum* to allay his thirst. The next day he began to make water freely, and could (p. 88) allow of being put into bed, but was raised high with pillows. Omit the infusion. That night he parted with six quarts of water, and the next night could lie down and slept comfortably. *July* 21st. he took a mild mercurial bolus. On the 25th. the diuretic effects of the *Digitalis* having nearly ceased, he was ordered to take three grains of the pulv. *Digital.* night and morning, for five days, and a draught with half an ounce of vin. chalyb. twice a day. *August* 15th. He took a purge of calomel and jallap, and some swelling still remaining in his legs, the *Digitalis* infusion was repeated. The water having been thus entirely evacuated, he was ordered saline draughts with acetum scilliticum and pills of salt of steel and extract of gentian. About a month after this, he returned home perfectly well.

Case CXXXIII

July 28th. Mr. A—— of W——, Aet. 29, became dropsical towards the close of a pulmonary consumption. He was ordered 12 grains of pulv. sol. cicutae and 1 of Digitalis twice a day. No remarkable effect took place.

Case CXXXIV

July 31. Mr. M——, Aet. 37. Hydrothorax. A single grain of sol. Digital. pulv. taken every night for three weeks cured him. The medicine never made him sick, but increased his urine, which became clear; whereas before it had been high coloured and turbid.

(p. 89) *Case CXXXV*

August 6th. Mr. C—— of B——, Aet. 42. Asthma and anasarca, the consequence of free living. He had been for some time under the care of an eminent physician of this place, but his complaints proving unusually obstinate, he consulted me. I directed an infusion of Digitalis to be taken every night, and a mixture with squill and tincture of cantharides twice a day. In about a week he became better, and continued daily mending. He has since enjoyed perfect health, having quitted a line of business which exposed him to drink too much.

Case CXXXVI

August 6th. Mr. M—— of C——, Aet. 44. Ascites and anasarca, preceded by symptoms of the epileptic kind. He was ordered to take two grains of pulv. Digitalis every morning, and three every night; likewise a saline draught with syrup of squills, every day at noon. His complaints soon yielded to this treatment, but in the month of November following he relapsed, and again asked my advice. The digitalis alone was now prescribed, which proved as efficacious as in the first trial. He then took bitters twice a day, and vitriolic acid night and morning, and now enjoys good health.

Before the Digitalis was prescribed, he had taken jallap purges, soluble tartar, salt of steel, vitriol of copper, &c.

(p. 90) *Case CXXXVII*

August 10th. Mrs. W—, Aet. 55. An anasarcaous leg, and sciatica; full habit. After bleeding and a purge, a blister was applied in the manner recommended by Cotunnius; and two grains of sol. Digital. with fifteen of sol. cicutae were directed to be taken night and morning. The medicine acted only as a diuretic; the pain and swelling of the limb gradually abated; and I have not heard of any return.

I must here bear witness to the efficacy of Cotunnius's method of blistering in the sciatica, having used it in a great number of cases, and generally with success.

Case CXXXVIII

August 16th. Mrs. A— of S—, Aet. 78. About the middle of Summer began to complain of short breath, great debility, and loss of appetite. At this time there were evident marks of effusion in the thorax, and some swellings in the legs. The advanced age, the weakness, and other circumstances of this patient, precluded every idea of her recovery; but something was to be attempted. Squills and other remedies had been tried; I therefore directed pills with two or three grains of the pulv. Digitalis to be taken every night for six nights, and a saline draught with forty drops of acetum scillit. twice in the day. She took but few of the draughts, seldom (p. 91) more than half one at a time, for they purged her, and she disliked them. The pills she took regularly, and with the happiest effect, for she could lie down, her breath was very much relieved, and a degree of appetite returned. *Sept.* 4th, some return of her symptoms demanded the further use of diuretics. I was afraid to push the Digitalis in so hazardous a subject, and therefore directed tinct. amara with tinct. canthar. and pills of squill, seneka, salt of tartar and gum ammoniac. These medicines did not at all check the progress of the disease, and on the 26th it became necessary to give the Digitalis again. The pills were therefore repeated as before, and infus. amarum with fixed alkaly ordered to be taken twice a day. The event was as favorable as before; and from this time she had no considerable return of dropsy, but languished

under various nameless symptoms, until the middle or end of November.

Case CXXXIX

Aug. 16th. Mrs. P—— of S——, Aet. 50. For a particular account of this patient, see Mr. Yonge's second Case.

Case CXL

Sept. 20th. B—— B——, Esq. A true spasmodic asthma of many years continuance. After every method of relief had failed; both under my management, and also under the direction of several of the ablest physicians of this kingdom; I was induced to (p. 92) give him an infusion of the Digitalis. It was continued until nausea came on but procured no relief.

Case CXLI

October 5th. Mr. R——, Aet. 43. (*The patient mentioned at No. 102.*) He had pursued his former mode of life, and had now a return of his complaints, with evident marks of diseased viscera. His belly not very large, but uncommonly tense. From this circumstance I did not expect the Digitalis to succeed, and therefore tried for some time to relieve him by the saline julep, with acet scillitic. jallap, mercury, syrup of squill, with aq. cinnam. decoction of Dandelion, &c.; but these being administered without advantage, I was driven to the Digitalis. As he was very weak and much emaciated, I only gave two grains night and morning for five days. As no increase of urine took place, I used alkaline salt with tinct. cantharieds:—This proving equally unsuccessful, on the 18th, I directed two ounces of the infusum Digitalis night and morning. This was continued until nausea took place, but the kidney secretion was not increased. Squill with opium, deobstruents of different kinds, sublimate solution, fixed alkaly, tobacco infusion, were now successively tried, but with the same want of success. The fullness of his belly made it necessary to tap him, and by repeating this operation he continued alive to the end of the year.

(p. 93) *Case CXLII*

October 19th. Mrs. R—, of B—, Aet. 47. Supposed Asthma, of eighteen months duration. She had kept her room for four months, and could not lie down without great disturbance; was very thin, and had totally lost all inclination for food. She was directed to take two gr. of pulv. sol. Digital. night and morning for five days, and infusum amarum, at the hours of eleven and five. In the course of a week she was much relieved, and could remain in bed all night. After a few days interval she took the Digitalis for five days more, and was soon after that well enough to come down stairs and conduct her family affairs.

In *April* 1785, she had a slight return, but not such as to confine her to her chamber. She experienced the same relief from the same medicine, but continuing it for seven days without interruption, it excited nausea.

Case CXLIII

October 28th. Mr. A—, subject to nephritis calculosa: After an attack of that kind, had still a troublesome sense of weight about his loins, now and then rising to pain, and a degree of dysuria, together with a want of appetite. These symptoms not readily yielding to the usual methods of treatment, I directed an infusion of Digitalis. The fourth dose (p. 94) caused a copious flow of urine; the sixth made him sick, and he was more or less sick at times for three days; but felt no more of his complaints.

I don't believe it is at all necessary to bring on sickness in these cases, but an unexpected absence from town prevented me from seeing him time enough to stop the exhibition of the medicine.

Case CXLIV

October 31st. Mrs. C—, of W—, Aet. 67. Asthma, and very thick hard legs of long continuance. The last month or two her breath worse than usual, her belly swollen, her thighs anasarcous, and her urine in small quantity. After trying garlic,

squill, and purgatives without advantage, I directed the Digital. Infus. After taking about five ounces, her urine from thick and turbid, changed to clear and amber coloured, its quantity considerably increased, and her breathing easy. Contrary to my orders, but impelled by the relief she had found, she finished the remaining three ounces of the infusion, which made her very sick, and the free flow of urine immediately ceased. No medicine was administered for a fortnight, during which time her complaints increased. I then directed an infusion of tobacco, which affected her head, but did not increase her urine. She had recourse again to the Digitalis infusion, which once more removed the fulness of the belly, reduced the swellings of her thighs, and relieved her breath, but had no effect upon her legs.

(p. 95) *Case CXLV*

Nov. 2d. Miss B—— of C——, Aet. 22. A very evident fluctuation in the abdomen, which was considerably distended, whilst the rest of her frame was greatly emaciated. The presence of cough, hectic fever, and other circumstances, made it probable that this apparent ascites was caused by a purulent, and not a watery effusion. However it was possible I might be mistaken; the Digitalis was therefore given, but without any advantage.

The further progress of the disease confirmed my first opinion, and she died consumptive.

Case CXLVI

Nov. 4th. Mr. P—— of M——, Aet. 40. Subject to troublesome nephritic complaints, and after the last attack did not recover, or void the gravelly concretions as usual, a sense of weight across his loins continuing very troublesome. The usual medicines failing to relieve him, I ordered four grains of pulv. Digital. to be taken every other night for a week, and fifteen grains of mild fixed vegetable alkaly to be swallowed twice a day in barley water. He soon lost all his complaints; but we must not in this case too hastily attribute the cure to the Digitalis, as the alkaly has also been found a very useful medicine in similar disorders.

(p. 96) *Case CXLVII*

Nov. 4th. Mr. B—— of N——, Aet. 60. Had been much subject to gout, but his constitution being at length unable to form regular fits, he became dropsical. Pulv. sol. Digital. in doses of two or three grains, at bed-time, gave him some relief, but did not perfectly empty him. About three months afterwards he had occasion to take it again; but it then produced no effect, and he was so debilitated that it was not urged further.

Case CXLVIII

Nov. 8th. Mr. G——, Aet. 35. In the last stage of a phthisis pulmonalis, was attacked with a most urgent and painful difficulty of breathing. Suspecting this distress might arise from watery effusion in the chest, I gave him Digitalis, which relieved him considerably; and during the remainder of his life his breath never became so bad again.

Case CXLIX

Nov. 13th. Mrs. A—— of W—— h——, Aet. 68. One of those rare cases in which no urine is secreted. It proved as refractory as usual to remedies, and not having ever succeeded in the cure of this disease, I determined to try the Digitalis. It was given in infusion, and, after a few doses, the secretion of a small quantity of urine seemed to justify the attempt. The next day, however, the secretion (p. 97) ceased, nor could it be excited again, tho' at last the medicine was pushed so as to occasion sickness, which continued at intervals for three days.

Case CL

Nov. 20th. Mrs. B——, Aet. 28. In the last stage of a pulmonary consumption became dropsical. I directed three grains of the pulv. Digital. to be taken daily, one in the morning, and two at night. She took twenty grains without any sensible effect.

Case CLI

Nov. 23d. Master W——, Aet. 7. Supposed hydrocephalus internus. A grain of pulv. sol. Digitalis was directed night and morning. After three days, no sensible effects taking place, it

was omitted, and the mercurial plan of treatment adopted. The child lived near five months afterwards. Upon dissection near four ounces of water were found in the ventricles of the brain.

Case CLII

Nov. 26th. Mrs. W——, Aet. 65. I had attended this lady last winter in a very severe peripneumony, from which she narrowly escaped with her life. When the cold season advanced this winter, she perceived a difficulty in breathing, which gradually became more and more troublesome. I found (p. 98) her much harrassed by a cough, which occasioned her to expectorate a little: the least motion increased her dyspnoea; she could not lie down in bed; her legs were considerably swelled, her urine small in quantity. I directed two grains of pulv. Digitalis made into a pill with gum ammoniac, to be taken every night, and to promote expectoration, a squill mixture twice in the day. Her urine in five days became clear and copious, and in a fortnight more she lost all her complaints, except a cough, for which she took the lac ammoniacum.

It is not improbable that the squill might have some share in this cure.

Case CLIII

December 7th. Mr. H——, Aet. 42. A large fat man, very subject to gravelly complaints. After an attack in the usual manner, continued to feel numbness in his lower limbs, and a sense of weight across his loins. I directed infusum Digitalis to be given every six hours. Six ounces made him sick, and he took no more. The next day his urine increased, a good deal of sand passed with it, and he lost his disagreeable feels, but the sickness did not entirely cease before the fourth day from its commencement.

(p. 99) *Case CLIV*

December 27th. Mr. B——, of H——, Aet. 55. Symptoms of hydrothorax, at first obscurely, afterwards more distinctly marked. Many things were tried, but the squill alone gave re-

lief. At length this failed. About the third month of the disease, a grain of pulv. Digital. was ordered to be taken night and morning. This produced the happiest effects. In *March* following he had some slight symptoms of relapse, which were soon removed by the same medicine, and he now enjoys good health. For a more particular narrative see case the first, communicated by Mr. Yonge.

Case CLV

December 31st. Mrs. B——, of E——, Aet. 50. An ovarium dropsy of long continuance. She took three grains of pulv. Digital. every night at bed time, for a fortnight, but without any effect.

Case CLVI

A poor man in this town, after his kidneys had ceased to secrete urine for several days, was seized with hickup, fits of vomiting, and transient delirium. After examination I was satisfied the disease was the same as that mentioned at CXLIX. A very experienced apothecary having tried various methods to relieve him, I despaired of any success, but determined to try the Digitalis. It was accordingly given (p. 100) in infusion. At first it checked the vomitings, but did not occasion any secretion of urine.

1785

The cases which have occurred to me in the course of this year, are numerous; but as the events of some of them are not yet sufficiently ascertained, I think it better to withhold them at present.

(p. 101) HOSPITAL CASES, UNDER THE DIRECTION OF THE
AUTHOR

The four following cases were drawn out at my request by Mr. Cha. Hinchley, late apothecary to the Birmingham Hospital. They are all the Hospital cases for which the Digitalis was prescribed by me, whilst he continued in that office.

Case CLVII

March 15th, 1780. John Butler, Aet. 30. Asthma and swelled legs. He was directed to take myrrh and steel every day, and three spoonfuls of infusum Digitalis every night. On the 8th of April he was discharged, cured of the swellings and something relieved of his asthmatic affections.

Case CLVIII

November 18th, 1780. Henry Warren, Aet. 60. This man had a general anasarca and ascites, and was moreover so asthmatic, that, neither being able to sit in a chair nor lie in bed, he was obliged constantly to walk about, or to lean forward against a window or table. You prescribed for him thus.

(p. 102) R. Aq. cinn. spt. oz. iv.

Oxymel. scillit.

Syr. scilit. aa. oz. i. m. cap. cochlear. larg. sexta quaque hora.

This medicine producing no increased discharge of urine, on the 25th you ordered the infusion of Digitalis, two spoonfuls every four hours. After taking this for thirty six hours, his urine was discharged in very great quantity; his breath became easy, and the swellings disappeared in a few days, though he took no more of the medicine. On the 2d of *December* he was ordered myrrh and lac ammoniacum, which he continued until the 23d, when he was discharged cured, and is now in good health.

Case CLIX

November 3d, 1781. Mary Crockett, Aet. 40. Ascites and universal anasarca. For one week she took sal. diureticus and tincture of cantharides, but without advantage. On the 10th you directed the infusion of Digitalis, a dram and half to half a pint, an ounce to be taken every fourth hour. Before this quantity was quite finished, the urine began to be discharged very copiously. The medicine was then stopped as you had directed. On the 15th, being costive, she took a jallap purge, and on the 24th she was discharged cured.

Case CLX

March 16th, 1782. Mary Bird, Aet. 61. Great fullness about the stomach; diseased liver, and anasaruous (p. 103) legs and thighs. For the first week squill was tried in more forms than one, but without advantage. On the 22d she began with the *Digitalis*, which presently removed all the swelling.

She was then put upon the use of aperient medicines and tonics, and on the first of *August* was discharged perfectly cured.

The three following Cases were drawn up and communicated to me by Mr. Bayley, who succeeded Mr. Hinchley as apothecary to the Hospital at Birmingham:

Shiffnal, April 26th, 1785.

Dear Sir,

DURING my residence in the Birmingham General Hospital, I had frequent opportunities of seeing the great effects of the *Digitalis* in dropsy. As the exhibition of it was in the following instances immediately under your own direction, I have drawn them up for your inspection, previous to your publishing upon that excellent diuretic. Of its efficacy in dropsy I have considerable evidence in my possession, but consider myself not at liberty to send you any other cases except those you had your self the conduct of. The *Digitalis* is a very valuable acquisition to medicine; and, I trust, it will cease to be dreaded when it is well understood.

I am, Sir, your obedient,
And very Humble servant,
W. BAYLEY

(p. 104) *Case CLXI*

Mary Hollis, aged 62, was admitted an out patient of the Birmingham General Hospital *February* 12th, 1784, labouring under all the effects of hydrothorax; her dread of suffocation during sleep was so great, that she always reposed in an elbow chair. She was directed to take two grains of *Digitalis* in powder every night and morning, and for a few days found great relief;

but, on the eighth day, as she had complained of sickness, and had been considerably purged, she was ordered to desist taking any more of her powders. On the 14th day she was ordered an ounce of the following infusion twice in a day: R. Sol. Digital. purp. sicc. drams iss. aq. bullient. lb. ss. digere per semi-horam, colaturae adde tinct. aromatic oz. i. This infusion did not purge, but sometimes excited nausea, though not sufficient to prevent her from continuing its use. She grew gradually better, and on the 6th of *May* was discharged perfectly cured. The diuretic effects of the *Digitalis* were in this instance immediate.

Case CLXII

Edward James, Aet. 21. Admitted *March* 20th, 1784. Complained of great difficulty of breathing, pain in his head, and tightness about the stomach, with a trifling swelling of his legs. Ordered pil. scillit. scruple i. ter de die. On the third day his legs much more swelled, his breathing more difficult, and in every respect worse; his pulse very small (p. 105) and quick, complained when he turned in bed, of something like watter rolling from one side of the thorax to the other. A remarkable blueness about the mouth and eyes, and purged considerably from the pil. scill. Ordered to omit the pills and to take oz.i. of infus. *Digitalis* every eight hours; the proportion drams iss. to eight ounces of water and oz.i. of aq. n. m. sp.—7th Day, The infusion had neither purged, nor vomited him: he only complained once or twice of giddiness. His belly was now very hard, rather black on the right side of the navel, and his legs amazingly swelled. Ordered a bolus with rhubarb and calomel, to be taken in the morning, and oz.ii. julep salin. cum tinct. canthar. gutt. forty ter die.—12th Day, nearly in the same state, except his breathing was somewhat more difficult, being now obliged to have his head considerably raised. Persistat—From this day to the 32d day he became hourly worse. His belly which at first was only hard, now evidently contained a large quantity of water, his legs were more swelled, and a large sphacelated sore appeared upon each outer angle. Respiration was so much obstructed, that he was obliged to sit quite upright to prevent suffocation. He made

very little water, not more than eight ounces in a day and a night, and was much emaciated. Ordered his purging bolus again, and oz.ii. of a mixture with sal diuretic, oz.ss. to oz.xii. three times in a day, and a poultice with ale grounds to his legs.

54th day. To this period there was not the least probability of his existing; his legs and thighs were (p. 106) one continued blubber, his thorax quite flat, and his belly so large that it measured within one inch as much as a woman's in this Hospital the day she was tapped, and from whom twenty seven pounds of coagulable lymph were taken. He made about three ounces of water in twenty-four hours: his penis and scrotum were astonishingly swelled, and no discharge from the sores upon his legs. Ordered to take a pill with two grains of powdered Fox-glove night and morning. For a few days no sensible effect, but about the 60th day he complained of being continually giddy, and had some little pain in his stomach. He now made much more water, and dared to sleep. His appetite which through the whole of his illness had been very bad, was also better. 66th day. Breathing very much relieved, the quantity of water he made was three chamber pots full in a day and a night, each pot containing two quarts and four ounces, moderately full. Ordered to continue his pills, and his legs which were very flabby, to be rolled.

69th day. His belly nearly reduced to its natural size, still made a prodigious quantity of water, his appetite very good, habit of body rather lax, and his complexion ruddy. On the 2d of *June*, being still rather weak, he was ordered decoct. cort. oz.ii. ter de die; and on the 12th was discharged from this Hospital perfectly cured.

W. BAYLEY.

(p. 107) Mr. Bayley's respectful compliments to Doctor Withering: he sends the case of Edward James, which he believes is pretty correct. He laments not having it in his power to send the measure of his belly, having unfortunately mislaid the tape: he heard from James yesterday, and he is perfectly well.

General Hospital, August 5, 1784.

Case CLXIII

On the 26th February, 1785, Sarah Ford, aged 42, was admitted an out-patient of the Birmingham General Hospital: she complained of considerable pain in her chest, and great difficulty of breathing, her face was much swelled and her thighs and legs were anasarcous. She had extreme difficulty in making water, and with many painful efforts she did not void more than six ounces in twenty-four hours. She had been in this situation about six weeks, during which time she had taken ammoniacum, olibanum, and large quantities of squills, without any other effect than frequent sickness. Upon her commencing an Hospital patient, the following medicine was exhibited. R. gum ammoniac drams ii. pulv. sol. Digital. purp. scruples ii. sp. lavand. comp. ut fiat pil. 40. cap. ii. nocte manequē. She continued the use of these pills for a few days, without any sensible effect. On the eighth day her breathing was much relieved, her legs and thighs were not so much swelled, and in a day and (p. 108) a night she made five pints of water. By the 12th day her legs and thighs were nearly reduced to their natural size. She continued to make water in large quantities, and had lost her pain in the thorax. To the 20th of *March*, she made rapid advances towards health, when not a symptom of disease remaining, she was discharged.

(p. 109) COMMUNICATIONS FROM CORRESPONDENTS

London, Norfolk-street,

May 31st, 1785.

SIR,

I HAD the favour of your letter last week; and I shall be very happy if I can give you any intelligence relating to the Foxglove, that can answer the purpose in which you are so laudably engaged.

It is true that my brother, the late Dr. Cawley, was greatly relieved, and his life, perhaps, prolonged for a year, by a decoction of the Foxglove root; but why it had not a more lasting effect, it is necessary I should tell you that he had all the signs of a dis-tempered viscera, long before any water swellings appeared; it was

manifest that his dropsy was merely symptomatic, and he could therefore only from time to time have any relief from medicine. In the year 1776, he returned from London to Oxon. having consulted several physicians at the former place, and Dr. Vivian at the latter, but without any success; and he was then told of a carpenter at Oxon. that had been cured of a Hydrops pectoris by the Foxglove root, and as he (p. 110) was a younger, and in other respects an healthy man, his cure, I believe, remains a perfect one.

I did not attend my brother whilst he took the medicine, and therefore I cannot speak precisely to the operation of it; but I remember, by his letters, that he was dreadfully sick and ill for several days before the secretion of urine came on, but which it did do to a greater degree; relieved his breath, and greatly lessened the swelling in his legs and thighs; but the two instances I have lately seen in this part of the world, are much stronger proofs of the efficacy of it than my brother's case.

I am, &c.

ROBERT CAWLEY.

N.B. Whenever I have another opportunity of giving the Foxglove, it shall be in small doses:—In which I should hope it might succeed, although it might be more slowly. If you should try it with success, I should be glad to know what mode you made use of.

Dr. Cawley's prescription

R. Rad. Digital. purpur. siccat. et contus. oz.ii.

Coque ex aq. fond. lb.ii. ad. lb.i. colat. liquor. adde aq. junip. comp. oz.ii.

Mell. anglic oz.i. m. fumat cochl. iv. omni nocte h. f. et mane.

(p. 111)—I have elsewhere remarked, that when the Digitalis has been properly given, and the diuretic effects produced, that an accidental over-dose bringing on sickness, has stopped the secretion of urine. In the present instance it likewise appears, that violent sickness may be excited, and continue for several days without being accompanied by a flow of urine; and it is probable that the latter circumstance did not take place, until

the severity of the former abated. If Dr. Cawley had not had a constitution very retentive of life, I think he must have died from the enormous doses he took; and he probably would have died previous to the augmentation of the urinary discharge. For if the root from which his medicine was prepared, was gathered in its active state, he did not take at each dose less than *twelve* times the quantity a strong man ought to have taken. Shall we wonder then that patients refuse to repeat such a medicine, and that practitioners tremble to prescribe it? Were any of the active and powerful medicines in daily use to be given in doses *twelve* times greater than they are, and these doses to be repeated without attention to the effects, would not the patients die, and the medicines be condemned as dangerous and deleterious?—Yet such has been the fate of Foxglove!

A Letter to the Author, from Mr. Boden, Surgeon, At
Broseley, in Shropshire

Broseley, 25th May, 1785.

Dear Sir,

HAVE inclosed the prescriptions that contained the sol. Digital. which I gave to Thomas Cooke and Thomas Roberts.

Thomas Cooke, Aet. 49, had been ill about two or three weeks. When I saw him he had no appetite, and a constant thirst: a fullness and load in the stomach: the thighs, legs and hands, much swell'd, and the face and throat in a morning; was costive, and made but little water, which was high coloured; the pulse very weak, and his breath exceeding bad. *June* 17th. R. Argent. viv dr.i. cons. cynosbat. scruples ii. fol. Digital. pulv. gr. xv. f. pil. xxiv. capt. ii. omni nocte hora decubitus. He was likewise purged by a bolus of agent. viv. jallap, Digit. elaterium and calomel, which was repeated on the fourth day, to the third time. From *June* 17th to the 29th, the symptoms were mostly removed, making water freely, and having plenty of stools; in a week after he was perfectly well, and remains so ever since. The cure was finished by steel and bitters.

Thomas Roberts, Aet. 40, had a deformed chest, was obliged to be almost in an erect posture when in bed; the other symptoms were nearly the same as Cooke's. *August* 3d. The pills prescribed *June* (p. 113) 17th for Cooke.—17th. A purging bolus of jalap and Digitalis, once a week. He continued the medicines till the latter end of *August*, when he got very well, but the complaint returned in *Jan.* worse than before. He is now much better, but I have great reason to believe the liver to be diseased.

I am, with greatest respect,

Your very obliged humble servant,

DANIEL BODEN.

P. S. The second patient, on his relapse, took Digitalis again, combined with other things.

CASE communicated by Mr. Causer, Surgeon, at Stour-bridge, Worcestershire

Mr. P—— of H—— M——, in the parish of Kingswinford, aged about 60; had been a strong healthy, robust, corpulent man; worked hard early in life at edge-tool making, and drank freely of strong malt liquor; for many years had been subject to gout in the extremities; for a few years past had been very asthmatic, and the gout in the extremities gradually decreased. When I first saw him which was *Sept.* 12, 1779, his legs were anasarcous, his belly much swelled, and an evident fluctuation of water. His breathing very bad, an irregular pulse, and unable to lie down. His easiest (p. 114) posture was standing with his body leaning over a chair, in which situation he would continue many hours together, labouring for breath, with the sweat trickling down his face very profusely; the urine in very small quantity. Diuretics of every kind I could think of were used with very little or no advantage. Blisters applied to the legs relieved very considerably for a time, but by no means could I increase the urinary discharge. Warm stomachic medicines were given, and at the same time sinapisms applied to the feet, in hopes of enticing gout to the extremities, but without any good effect.—*November* 22d. The swelling considerably increasing, an emetic of acet. scillitic. was given, which acted very violently, and increased the

urinary discharge considerably. He continued better and worse, using different kinds of diuretic and expectorating medicines until *September* 1781, when the disease was so much worse, I did not expect he could live many days. The acet. scillitic. was repeated, a table spoonful every half hour, till it acted briskly upwards and downwards; but without increasing the urinary discharge.—On the 17th of *September* I infused dr. iii. of the sol. Digitalis in oz. vi. of boiling water, for four hours; then strained it, and added oz. i. of tinct. aromatica.—On the 18th he began by taking one spoonful, which he was to repeat every half hour, till it made him very sick, unless giddiness, loss of sight, or any other disagreeable effect took place. I had never given the medicine before, and had prepared him to expect the operation to be very severe. I saw him again on the 21st; he (p. 115) had taken the medicine regularly, till the whole quantity was consumed, without perceiving the least effect of any kind from it, and continued well till the evening of the following day, when a little sickness took place, which increased, but never so as to occasion either vomiting or purging, but a surprising discharge of urine. The saliva increased so as to run out of his mouth, and a watery discharge from his eyes; these discharges continued, with a continual sickness, till the swelling was totally gone, which happened in three or four days. He afterwards took steel and bitters; and continued very comfortably, without any return of his dropsy, until the 7th of *April* 1782, when he was seized with an epidemic cough, which was very frequent with us at that time. His swellings now returned very rapidly, with the greatest difficulty in breathing, and he died in a few days. Blisters and expectorating medicines were used on this last return.

Extract of a letter from Mr. Causer

Mrs. S—, the subject of the following case, was as ill as it is possible for woman to be and recover; from the inefficacy of the medicines used, I am convinced no medicine would have saved her but the Digitalis. I never saw so bad a case recovered; and it shews, that in the most reduced state of body, the medicine in small doses, will prove safe and efficacious.

(p. 116) N.B. The Digitalis, in pills, never occasioned the least sickness. She took two boxes of them.

Case

January 2d, 1785. Mrs. S—, of W—, near Kidderminster, aged 38, has been affected with dropsical swellings of her legs and thighs, about six weeks, which have gradually grown worse; has now great difficulty in breathing, which is much increased on moving; a very irregular, intermittent pulse, urine in very small quantity, and in the seventh month of her pregnancy: a woman of very delicate constitution, with tender lungs from her infancy, and very subject to long continued coughs.

R. Pulv. scillae gr. iii.

Jalap gr. x. syr. rosar. solut. tinct. fenn. aa dr. ii. aq. menth. v. simpl. oz. iss. m. mane fumend.

R/ Pulv. scillae scruple i. G. ammoniac. sapon. venet. aa drams iss. syr. q. f. f. pilul. 42 cap. iii. nocte manequē.

On the 7th found her worse, and the swelling increased; the urine about oz. x. in the twenty-four hours.

R. Sol. sicc. Digital. dr. iii. coque in. aq. fontan. oz. xii. ad oz. vi. cola et adde. aq. juniper. comp. oz. ii. sacchar. alb. oz. ss. m. cap. cochlear. i. larg. 4tis horis.

(p. 117) She took about three parts of the medicine before any effect took place. The first was sickness, succeeded by a considerable discharge of urine. She continued the medicine till the whole was consumed, which caused a good deal of sickness for three or four days.

I saw her again on the 12th. The quantity of urine was much increased, and the swelling diminished. Pulse and breathing better.

R. Sol. sicc. Digital. G. assafetid. aa dr. i. calomel. pp. gr. x. sp. lavand. comp. q. s. siat pilul. xxxii. cap. ii. omni nocte hora somni.

A plentiful discharge of urine attended the use of these pills, and she got perfectly free from her dropsical complaints.

March 15th she was delivered: had a good labour, was treated as is usual, except in not having her breasts drawn, not intending

she should suckle her child, being in so reduced a state. Continued going on well till the 18th, when she was seized with very violent pains across her loins, at times so violent as to make her cry out as much as labour pains. Enema cathartic. fot. papav. applied to the part.

R. Pulv. ipecacoan. gr. vi. opii. gr. iv. syr. q. s. fiat. pilul. vi. capt. i. 2da quaque hora durante dolore.

(p. 118) R. Julep. e camphor. sp. minder. aa oz.ii. capt. cochlear. i. larg. post singul. pilul.

19th. Breathing short, unable to lie down, very irregular low pulse scarcely to be felt, fainty, and a universal cold sweat: no appetite nor thirst, spasmodic pains at times across the loins very violent, but not so frequent as on the preceding day.

R. Gum ammoniac. assafetid. aa dr. i. camphor. gr. xii. fiat pilul. 24. capt. ii. 3tia quaque hora in chochlear. ii. mixtur. seq.

R. Balsam. peruv. dr. iii. mucilag. G. arab. q. s. flor. zinci g. vi. aq. menth. simp. lb. ss. m.

Applic. Emp. vesicat. femorib. internis.

R. Sp. vol. foetid, elixir. paregor. balsam. Traumatic. aa dr. iii. capt. cochlear. parv. urgente languore.

20th. Much the same; makes very little water, and the legs begin to swell.—Applic. Emp. e pice burgund. lumbis.

23d. The swelling very much increased.—Capt. gutt. xv. acet. scillitic. ter die in two spoonfuls of the following mixture.

R. Infus. baccar. juniper. oz. vi. tinct. amar. tinct. stomachic. aa oz. i. m.

(p. 119) 25th. Much the same.

28th. The swelling considerably increased, in other respects very much the same.

30th. Breathing very bad, with cough and pain across the sternum, unable to lie down, legs, thighs, and body very much swelled, urine not more than four or five ounces in the twenty-four hours; hot and feverish, with thirst.

Applic. Emp. vesicat. stomacho et sterno.

R. G. assafetid. scruples ii. pulv. jacob. scruples i. rad. scill.

recent. gr. xii. extract. thebaïc. gr. iv. f. pilul. xvi. cap. iv. omni nocte.

R. Sal. nitr. sal. diuretic. aa dr. ii. pulv. e contrayerv. comp. dr. i. sacchar. oz. i. emuls. commun. lb. i. aq. cinnam. simpl. oz. i. m. capt. cochlear. iv. ter die.

April 2d. Much the same, no increase of urine.

3d. Breathing much relieved by the blister, which runs profusely. Repeated the medicines, and continued them till the 12th. The cough very bad, pulse irregular, swelling much increased, urine in very small quantity, not at all increased; great lowness and fainting. She desired to have some of the pills which relieved (p. 120) her so much when with child. I was almost afraid to give them, but the inefficacy of the other medicines gave me no hopes of a cure from continuing them, which made me venture to comply with her request.

R. Fol. siccat. Digital. G. assafetid. aa dr. i. sp. lavand. comp. q. s. s. pilul. xxxii. cap. ii. omni mane; et omni nocte cap. pilul. e styrace gr. vi.

17th. Considerable increase of urine.

21st. Swelling a good deal diminished; urine near four pints in twenty-four hours, which is more than double the quantity she drinks.

Applic. Emp. vesicat. femoribus internis.

The Digitalis pills and opiate at bed-time continued. Takes a tea cup of cold chamomile tea every morning.

25th. Swelling much diminished, makes plenty of water, appetite much mended, cough and breathing better. She omitted the medicine for three days; the urine began to diminish, the swelling and shortness of breathing worse. On repeating it for two days, the discharge was again augmented, and a diminution of the swelling succeeded. She has continued the pills ever since till the 14th of (p. 121) *May*; the dropsical symptoms and cough are entirely gone, the water is in sufficient quantity, her strength is recovered, and she has a good appetite. All she now complains of is a weight across her stomach, which is worse at times, and she thinks, unless it can be removed, she shall have a return of her dropsy.

Extract of a Letter from Doctor Fowler, Physician,
at Stafford

I UNDERSTAND you are going to publish on the Digitalis, which I am glad to hear, for I have long wished to see your ideas in print about it, and I know of no one (from the great attention you have paid to the subject) qualified to treat on it but yourself. There are gentlemen of the faculty who give verbal directions to poor patients, for the preparing and taking of an infusion or decoction of the green plant. Would one suppose that such gentlemen had ever attended to the nature and operation of a sedative power on the functions, *particularly* the *vital*? Is not such a vague and unscientific mode of proceeding putting a two edged sword into the hands of the ignorant, and the most likely method to damn the reputation of any very active and powerful medicine? And is it not more than probable that the *neglect* of adhering to a *certain* and regular preparation of the nicotiana, and the *want* (of what you *emphatically* call) a *practicable* dose, have been the chief causes of the once rising reputation of (p. 122) that noted plant being damned above a century ago? In short, the Digitalis is beginning to be used in dropsies, (although some patients are said to go off suddenly under its administration) somewhat in the style of broom ashes; and, in my humble opinion, the public, at this very instant, stand in great need of your *precepts*, *guards*, and *cautions* towards the safe and successful use of such a powerful sedative diuretic; and I have no doubt of your minute attention to those particulars, from a regard to the good and welfare of mankind, as well as to your own reputation with respect to that medicine.

I remember an officer in the Staffordshire militia, who died here of a dropsy five years ago. The Digitalis relieved him a number of times in a wonderful manner, so that in all probability he might have obtained a radical cure, if he would have refrained from hard drinking. I understood it was first ordered for him by a medical gentleman, and its sedative effects proved so mild, and diuretic operation so powerful, that he used to prepare it afterwards for himself, and would take it with as little ceremony as he would his tea. It is said, that he was so certain of its suc-

cessful operation, that he would boast to his bacchanalian companions, when much swelled, you shall see me in two days time quite another man.

CASES communicated by Mr. J. Freer, jun. Surgeon, in
Birmingham.

Case I

Nov. 1780. Mary Terry, aged 60. Had been subject to asthma for several years; after a severe fit of it her legs began to swell, and the quantity of urine to diminish. In six weeks she was much troubled with the swellings in her thighs and abdomen, which decreased very little when she lay down: she made not quite a pint of water in the twenty-four hours. I ordered her to take two spoonfuls of the infusion of Foxglove every three hours. By the time she had taken eight doses her urine had increased to the quantity of two quarts in the day and night, but as she complained of nausea, and had once vomited, I ordered the use of the medicine to be suspended for two days. The nausea being then removed, she again had recourse to it, but at intervals of six hours. The urine continued to discharge freely, and in three weeks she was perfectly cured of her swellings.

Case II

December, 1782. A poor woman, who had been afflicted with an ague during the whole of her pregnancy, and for two months with dropsical swellings of the feet, legs, thighs, abdomen, and labia pudenda; was at the expiration of the seventh month (p. 124) taken in labour. On the day after her delivery the ague returned, with so much violence as to endanger her life. As soon as the fit left her, I began to give her the red bark in substance, which had the desired effect of preventing another paroxysm. She continued to recover her health for a fortnight, but did not find any diminution in the swellings; her legs were now so large as to oblige her to keep constantly on the bed, and she made very little water. I ordered her the infusion of Foxglove three times a day, which, on the third day, produced a very copious discharge of urine, without any sickness; she continued the use

of it for ten days, and was then able to walk. Having lost all her swellings, and no complaint remaining but weakness, the bark and steel completed the cure.

Extract of a Letter from Doctor Jones, Physician, in Lichfield

ANXIOUS to procure authentic accounts from the patients, to whom I gave the Foxglove, I have unavoidably been delayed in answering your last favour. However, I hope the delay will be made up by the efficacy of the plant being confirmed by the enquiry. Long cases are tedious, and seldom read, and as seldom is it necessary to describe every symptom; for every case would be a history of dropsy. I shall therefore content myself with specifying (p. 125) the nature of the disease, and when the dropsy is attended with any other affection shall notice it.

Two years have scarcely elapsed since I first employed the Digitalis; and the success I have had has induced me to use it largely and frequently.

Case I

Ann Willott, 50 years of age, became a patient of the Dispensary on the 11th of April 1783. She then complained of an enlargement of the abdomen, difficulty of breathing, particularly when lying, and costiveness. She passed small quantities of high-coloured urine; and had an evident fluctuation in the belly. Her legs were oedematous. Chrystals of tartar, squills, &c. had no effect. The 13th of *June* she took two spoonfuls of a decoction of Foxglove, containing three drams of the dry leaves, in eight ounces, three times a day. Her urine soon increased, and in a few days she passed it freely, which continued, and her breath returned.

Case II

Mr. —, 45 years of age, had been long subject to dropsical swellings of the legs, and made little water. Two spoonfuls of the same decoction twice a day, soon relieved him.

Case III

Mrs. —, aged 70 years. A lady frequently afflicted with the gout, and an asthmatical cough. After a long continuance of the latter, she had a great diminution of urine, and considerable difficulty of breathing, particularly on motion, or when lying. Her body was much bound. There was, however, no apparent swelling. She took three spoonfuls of an aperient decoction of forty-five grains in six ounces and a half, every other morning. The urine was plentiful those days, and her breathing much relieved. In two or three weeks after the use of it she was perfectly restored. The purgative medicine neither increased the urine, nor relieved the breathing, till the Foxglove was added.

This spring she long laboured with the gout in her stomach, which terminated in a fit in her hand. During the whole of this tedious illness, of nearly three months, she passed little urine, and her breathing was again short.

She took the same preparation of Foxglove without any diuretic effect, and afterwards two and three grains of the powder twice a day with as little. The dulcified spirits of vitriol, however, quickly promoted the urinary secretion.

(p. 127) Case IV

Mr. C—, 46 years of age, had dropsical swellings of the legs, and passed little urine. He took the decoction with three drams, and was soon relieved.

Case V

Lady —, took three grains of the dried leaves twice a day, for swelled legs, and scantiness of urine, without effect.

Case VI

Mrs. Slater, aged 36 years. For dropsy of the belly and legs, and scantiness of urine, of several weeks standing, took three grains of the powder twice a day, and was quite restored in ten days. She took many medicines without effect.

Case VII

Mrs. P——, in her 70th year, took three grains of the powder twice a day, for scantiness of urine, and swelled legs, without effect.

Case VIII

Ann Winterleg, in her 26th year, had dropsical swellings of the legs, and passed little urine: she was relieved by two drams, in an eight ounce decoction.

(p. 128) Case IX

William Brown, aged 76. In the last stage of dropsy of the belly and legs, found a considerable increase of his urine by a decoction of Foxglove, but it was not permanent.

Case X

Mr. —, — years of age, and of very gross habit of body, became highly dropsical, and took various medicines, without effect. One ounce of the decoction, with three drams of the dry leaves in eight ounces, twice or three times a day, increased his urine prodigiously. He was evidently better, but a little attendant nausea overcame his resolution, and in the course of some weeks afterwards he fell a victim to his obstinacy.

Case XI

Mrs. Smith, about 50 years of age, after a tedious illness of many weeks, had a jaundice, and became dropsical in the legs. Two spoonfuls of the decoction, with three drams twice a day, increased her urine, and abated the swelling.

Case XII

Widow Chatterton, about 60 years of age. Took the decoction in the same way for dropsy of the legs, with little effect.

(p. 129) Case XIII

—— Genders, about thirty-four years of age, was delivered of three children, and became dropsical of the abdomen. She passed little or no urine, had constant thirst, and no appetite.

She took two spoonfuls of an eight ounce decoction, with three drams twice a day. By the time she had finished the bottle, (which must have been on the fourth day,) she had evacuated all her water, and could go about. Her appetite increased with every dose, and she recovered without farther help.

Case XIV

Miss M—— M——, in her 20th year. Had been infirm from her cradle, and, after various sufferings, had an astonishing oedematous swelling of one leg and thigh, of many weeks standing. She passed little or no urine, and had all her other complaints. She took 2 spoonfuls of an eight oz. decoction of two drams, twice a day. Her urine immediately increased; and, on the third day, the swelling had entirely subsided.

Case XV

Mr. P——, 65 years of age, and of a full habit of body. Had lived freely in his youth, and for many years led rather an inactive life. His health was much impaired several months, and he had a considerable distention, and evident fluctuation in (p. 130) the abdomen, and a very great oedema of the legs and thighs. His breathing was very short, and rather laborious, appetite bad, and thirst considerable. His belly was bound, and he passed very small quantities of high-coloured urine, that deposited a reddish matter. He had taken medicines some time, and, I believe, the *Digitalis*; and had been better.

A blister was applied to the upper and inside of each thigh; he took two spoonfuls of the decoction, with three drams of the dry leaves, two or three times a day; and some opening physic occasionally.

He lived at a considerable distance, and I did not visit him a second time; but I was well informed, about ten days or a fortnight afterwards, that his urine increased amazingly upon taking the decoction, and that the water was entirely evacuated.

Case XVI

Mrs. G——, aged 50 years. After being long ailing, had a large collection of water in the abdomen and lower extremities.

Her urine was high-coloured, in small quantities, and had a reddish sediment. She took the decoction of Digitalis, squills, &c. without any effect. The chrystals of tartar, however, cured her speedily.

(p. 131) *Case XVII*

Mr. —, about 50 years of age, complained of great tension and pain across the abdomen, and of loss of appetite; his urine, he thought, was less than usual, but the difference was so trifling he could speak with no certainty: his belly seemed to fluctuate. Among other things he tried the Foxglove leaves dried, twice a day; and, although it appeared to afford him relief, yet the effect was not permanent.

Case XVIII

Mr. W—, aged between 60 and 70 years; and rather corpulent: was considerably dropsical, both of the belly and legs, and his urine in small quantities. Three grains of the dry leaves, twice a day, evacuated the water in less than a fortnight.

Case XIX

Sarah Taylor, 40 years of age, was admitted into the Dispensary for dropsy of the abdomen and legs; and was relieved by the Decoctum digitalianum.

Case XX

Lydia Smith, aged 60. Dispensary. Laboured many years under an asthma, and became dropsical. She took the decoction without effect.

(p. 132) *Case XXI*

John Leadbeater, aged 15 years. Had a quotidian intermittent, which was removed by the humane assistance of an amiable young lady. His intermittent was soon attended by a very considerable ascites; for which he became a patient of the Dispensary. He took a decoction of Foxglove night and morning. His urine increased immediately, and he lost all his complaints in four days.

Case XXII

William Millar, aged 50 years. Admitted into the Dispensary for a tertian ague, and general dropsy. The dropsy continuing after the ague was removed, and his urine being still passed in quantities; he took the powdered leaves, and recovered his health in five days.

Case XXIII

Ann Wakelin, 10 years of age. Had for several weeks a dropsy of the belly after an ague. She took a decoction of Foxglove, which removed all complaint fy the fourth day.

Case XXIV

Ann Meachime; a Dispensary patient. Had an ascites and scantiness of urine. She took the powder (p. 133) of Foxglove, and evacuated all her water in three days.

It may not be improper to observe, 1st. That various diuretics had long been given in many of these cases before I was consulted. And, 2dly. That the exhibition of the Foxglove was but seldom attended with sickness.

Remarks

These Cases, thus liberally communicated by my friend, Dr. Jones, are more acceptable, as they seem to contain a faithful abstract from his notes, both of the unsuccessful as well as the successful Cases.

The following Tabular View of them will give us some Idea of the efficacy of the Medicine.

Anasarca.....	7 Cases	{ Cured, 3 Relieved, 1 Failed, 3
Ascites.....	5 Cases	{ Cured, 4 Relieved, 1
Oedematous leg.....	1 Case	—Cured, 1
Ascites and anasarca.....	7 Cases	{ Cured, 4 Relieved, 2 Failed, 1

Asthma and dropsy.....1 Case—Failed, 1
 Hydrothorax and gout.....1 Case—Cured, 1
 —, ascites and anasarca.....2 Cases—Cured, 2

(p. 134) A CASE of anasarca communicated by Mr. Jones,
 Surgeon, in Birmingham

DEAR SIR,

HAVING lately experienced the diuretic powers of the Foxglove, in a case of anasarca; I do myself the pleasure of communicating a short history of the treatment to you.

I am, &c.

W. JONES.

Birmingham,

May 17th, 1785.

My patient, Mrs. C——, who is in her 51st year, had the following symptoms, viz. alternate swellings of the legs and abdomen, a little cough, shortness of breath in a morning, thirst, weak pulse, and her urine, which was so small in quantity as seldom to amount to half a pint in twenty-four hours, deposited a clay-coloured sediment.

April 16th, 1785, I directed the following form:

R. Sol. Digitalis siccat. dr. ii.

Aq. fontanae bullient. oz. viii. s. infus. et cola.

Summat cochl. larga iii. o. n. et mane.

On the 17th she had taken twice of the infusion, and though by mistake only two teaspoonfuls for a (p. 135) dose, yet the quantity of urine was increased to about a pint in the twenty-four hours. She was then directed to take two tablespoonfuls night and morning. And,

On the 18th, a degree of nausea was produced. A pint and half of urine was made in the last twenty-four hours. During the time above specified she had two or three stools every day. The infusion was now omitted.

On the 19th the swellings of the legs was removed. A degree of nausea took place in the morning, and increased so much during the day, that she vomitted up all her food and medicine. As she was very low, and complained of want of appetite, a cordial

julep was directed to be taken occasionally, as well as red port and water, mint tea, &c. She informed me that whatever she took generally staid about an hour before it came up again, and that the mint tea staid longest on the stomach. The vomiting decreased gradually, and ceased on the 22d. The discharge of urine remained considerable during the three following days, but its quantity was not measured.

22d. A dose of neutral saline julep was directed to be taken every fourth hour.

On the 23d she complained of thirst, and thought the discharge of urine not so copious as on the preceding days, therefore the saline julep was continued (p. 136) every fourth hour, with the addition of thirty drops of the following medicine:

R. Aceti scillitic. dr. vi.

Tinct. aromat. dr. ii.

Tinct. thebaic. gutt. xx. m.

The bowels have been kept open from the 19th, by the occasional use of emollient injections.

On the 24th the legs were much swelled again; she complained of languor and a degree of nausea. The discharge of urine increased a little since the 23d. Her pulse was low and her tongue white. The urine, which had been rendered clear by the infusion of Foxglove, now deposited a whitish sediment.

On the 25th her appetite began to return, the swelling of the legs diminished, and she thought herself much relieved. The urine was considerable in quantity, and clear.

On the 26th she was thirsty and languid. The swelling was removed; the quantity of urine discharged in the last twenty-four hours was about a pint. She continued to mend from this time, and is now in good health.

A giddiness of the head, more or less remarkable at times, was observed to follow the use of the Foxglove, and it lasted nine or ten days.

(p. 137) This is the second time that I have relieved this patient by the infusion of Foxglove. I used the same proportion of the fresh leaves the first time as I did of the dried ones the last. The violent vomiting which followed the use of the in-

fusion made with the dried leaves, did not take place with the fresh, though she took near a pint made with the same proportion of the herb fresh gathered.

Remarks

THE above is a very instructive case, as it teaches us how small a quantity of the infusion was necessary to effect every desirable purpose. At first sight it may appear from the concluding paragraph, that the green leaves ought to be preferred to the dried ones, as being so much milder in their operation; but let it be noticed, that the same quantity of infusion was prepared from the same weight of the green as of the dried leaves, and consequently, as will appear hereafter, the infusion with the dried leaves was five times the strength of that before prepared from the green ones. We need not wonder, therefore, that the effects of the former were so disagreeable, when the dose was five times greater than it ought to have been. But what makes this matter still more obvious, is the mistake mentioned at first, of two tea spoonfuls only being given for a dose. Now a tea spoonful, containing about a fourth or a fifth part of the contents of a table spoon, the dose then given, was very nearly the same as that which had before been taken of the (p. 138) infusion of the green leaves, and it produced precisely the same effects for it increased the urinary discharge, without exciting the violent vomiting.

Letter from DOCTOR JOHNSTONE, Physician, in Birmingham

DEAR SIR,

THE following cases are selected from many others in which I have given the *Digitalis purpurea*; and from repeated experience of its efficacy after other diuretics have failed, I can recommend it as an effectual, and when properly managed, a safe medicine.

I am, &c.

E. JOHNSTONE.

Birmingham, May 26,

1785.

March 8th, 1783, I was called to attend Mr. G——, a gentleman of robust habit, who had led a regular and temperate life. Aet.

68. He was affected with great difficulty of respiration, and cough particularly troublesome on attempting to lie down, oedematous swellings of the legs and thighs, abdomen tense and sore on being pressed, pain striking from the pit of the stomach to the back and shoulders; almost constant nausea, especially after taking food, which he frequently threw up; water thick and high-coloured, passed with difficulty and in (p. 139) small quantity; body costive; pulse natural; face much emaciated, eyes yellow and depressed. He had been subject to cough and difficulty of breathing in the winter for several years; and about four years before this time, after being exposed to cold, was suddenly deprived of his speech and the use of the right side, which he recovered as the warm weather came on; but since that time had been remarkably costive, and was in every respect much debilitated. He first perceived his legs swell about a year ago; by the use of medicines and exercise, the swellings subsided during the summer, but returned on the approach of winter, and gradually increased to the state in which I found them, notwithstanding he had used different preparations of squills and a great variety of other diuretic medicines. I ordered the following mixture.

R. Foliorum Digitalis purpur. recent. dr. iii. decoque ex aq. fontan. oz. xii ad oz. vi colaturae adde Tinctur. aromatic. Syr. zinzib. aa oz. i. m. capt. cochl. duo larga secunda quaque hora ad quartam vicem nifi prius nausea supervenerit.

March 9th. He took four doses of the mixture without being the least sick, and made, during the night upwards of two quarts of natural coloured water.

(p. 140) 10th. Took the remainder of the mixture yesterday afternoon and evening, and was sick for a short time, but made nearly the same quantity of water as before, the swellings are considerably diminished, his appetite increased, but he is still costive.

R. Argent. viv. balsam peruv. aa dr. ss. tere ad extinctionem merc. et adde cum. ammon. scruples iii. aloes socotorin. dr. ss. rad. scil. recent. scruples ss. syr. simpl. q. s. s. mass. in pil. xxxii divid. cap. iii. bis in die.

14th. Continued to make water freely. The swellings of

his legs have gradually decreased; soreness and tension of the abdomen considerably less.

Omittant. pil. cap. mistur. c. decoct. Digitalis &c. 3tia quaque hora ad 3tiam vicem.

15th. Made a pint and a half of water last night, without being in the least sick, and is in every respect considerably better. Repet. Pillul. ut antea.

21st. Makes water as usual when in health, and the swellings are entirely gone.

R. Infus. amar. oz. v. tinctur. Rhei spirit. oz. ii. spirit vitriol. dulc. dr. ii. syr. zinzib. dr. vi. m. cap. cochl. iii. larg. ter in die.

He soon gained sufficient strength to enable him to go a journey, and returned home in much better (p. 141) health than he had been from the time he was affected with the paralytic stroke, and excepting some return of his asthmatic complaint in the winter, hath continued so ever since.

Case II

R— Howgate, a man much addicted to intemperance, particularly in the use of spirituous liquors, Aet. 60, was admitted into the Hospital near Birmingham, May 17, 1783. He complained of difficulty of breathing, attended with cough, particularly troublesome on lying down; drowsiness and frequent dozing, from which he was roused by startings, accompanied with great anxiety and oppression about the breast, oedematous swellings of the legs; constant desire to make water, which he passed with difficulty, and only by drops; pulse weak and irregular; body rather costive; face much emaciated; no appetite for food.—Cap. pil. scil. iii. ter in die.*

May 20th. The pils have had no effect.—Cap. mistur. c.† Decoct. Digital. &c. cochl. ii. larg. 3tia quaque hora, ad 3tiam vicem.

May 21st. Made near two quarts of water in the night, without being in the least sick. He continued (p. 142) the use of the mixture three times in the day till the 30th, and made about

* R. Rad. scil. recent. sapon. castiliens. pulv. Rhei opt. aa. scruples i. ol. junip. gutt. xvi. syr. bals. q. s. f. mass. in pil. xxiv. divid.

† Prepared in the same manner as in the former case.

three pints of water daily, by which means the swellings were entirely taken away; and his other complaints so much relieved, that on the 6th of June he was dismissed free from complaint, except a slight cough. But returning to his old course of life, he had had frequent attacks of his disorder, which have been always removed by using the Digitalis.

Extract of a letter from MR. LYON, Surgeon, at Tamworth

—Mr. Moggs was about 54 years of age, his disease a dropsy of the abdomen, attended with anasarca swellings of the limbs, &c. brought on by excessive drinking. I believe the first symptoms of the disease appeared the beginning of November, 1776; the medicines he took before you saw him, were squills in different forms, sal diureticus and calomel, but without any good effect; he begun the Digitalis on the 10th of July 1777; a few doses of it caused a giddiness in the head, and almost deprived him of sight, with very great nausea, but very little vomiting, after which a considerable flow of urine ensued, and in a very short time, a very little water remained either in the cavity of the abdomen, or the membrana adiposa, but he remained excessive weak, with a fluttering pulse at the rate of 150 or frequently 160 in a minute; he kept pretty free from water for upwards of twelve months; it then (p. 143) collected, and neither the Digitalis nor any other medicine would carry it off. I tapped him the 2d of August 1779 in the usual place, and took some gallons of water from him, but he very soon filled again, and as he had a very large rupture, a considerable quantity of the water lodged in the scrotum, and could not be got away by tapping in the usual place. I therefore (on the 28th of the same month) made an incision into the lower part of the scrotum, and drained off all the water that way, but he was so very much reduced, that he died the 8th or 9th of *September* following, which was about two years and two months after he first begun the Digitalis.

I have had several dropsical patients relieved, and some perfectly recovered by the Digitalis, since you attended Mr. Moggs, but as I did not take any notes or make any memorandums of them, cannot give you any of them.

Communications from DR. STOKES, Physician, in Stourbridge

DEAR SIR,

I ACCEPT with pleasure your invitation to communicate what I know respecting the properties of *Digitalis*; and if an account of what others had discovered before you,* with a detail (p. 144) of my own experience, shall be allowed the merit of at least a well meant acknowledgment, for the early communication you were so kind to make me, of the valuable properties you had found in it; I shall consider my time as well employed. A knowledge of what has been already done is the best ground work of future experiment; on which account I have been the more full on this subject, in hopes that given with the cautions which you mean to lay down in the cure of dropsies, it may prove alike useful in that of other diseases, one of which stands foremost among the *opprobria* of medicine.

Case I.

Mrs. M——. Orthopnea, pain, and excessive oppression at the bottom of the sternum. Pulse irregular, with frequent intermissions. Appetite very much impaired. Legs anasarcous.

Empl. vesicator. pectori dolent.

Infus. Digital. e dr. iii. ad. aq. ℥c. oz. viii. cochl. j. o. h. donec nausea excitetur vel diuresis satis copiosa proveniat.

I ordered it of the above strength, and to be repeated often, on account of the great emergency of the case, but the nausea excited by the first dose prevented its being given at such short intervals. A 3d dose I found had been given, which was followed by vomitings. All her complaints gradually abated, (p. 145) but in about a fortnight recurred, notwithstanding the use of *infus. amar. &c.*

Dec. 2. Intus. Digit. e. dr. iss. ad. aq. ℥c. oz. viii. cochl. ii. horis ℥c. u. a.

Complaints gradually abated, swellings of the legs nearly gone down.

* See this account in the Introduction.

About a month afterwards you was desired to visit this patient.*

1785

Case

Jan. 5th. Mrs. M——, Aet. 48. Hydrothorax and anasar-
cous legs, of eight months duration. She had taken jallap,
squill, salt of tartar, and various other medicines. I found her
in a very reduced state, and therefore directed only a grain and
half of the Pulv. Digital. to be given night and morning. This
in a few days encreased the secretion of urine, removed her diffi-
culty of breathing, and reduced the swelling of her legs, without
any disturbance to her system.

Three months afterwards, a severe attack of gout in her legs
and arms, removing to her head, she died.

Dr. Stokes had an opportunity of examining the dead body,
and I had the satisfaction to learn from him, that there did not
appear to have been any return of the dropsy.

(p. 146) On the examination of the body I noticed, among
others, the following appearances.

About $\frac{3}{4}$ oz. of bloody water flowed out, on elevating the
upper half of the scull, and a small quantity also was found at the
base.

BRAIN. Blood-vessels turgid with blood, and many of those
of considerable size distended with air.

A very slight watery effusion between the *Pia Mater* and
Tunica arachnoidea. About $\frac{3}{4}$ oz. of watery fluid in the
lateral ventricles.

THORAX. In the left cavity about 4 oz. of bloody serum; in
the right but little. Lungs, the hinder parts loaded with blood.
Adhesions of each lobe to the pleura. *Pericardium* containing
but a very small quantity of fluid. *Heart* containing no coagula
of blood. *Valves of the Aorta* of a cartilaginous texture, as if
beginning to ossify.

* For reasons assigned at p. 100, I did not intend to introduce any case, occurring under
my own inspection, in the course of the present year; but it may be satisfactory to con-
tinue the history of this disease, as Dr. Stokes's narrative would otherwise be incomplete.

Abdominal Viscera natural, and a profusion of *Fat* under the integuments of the abdomen and thorax, in the former to the thickness of an inch and upwards, and in very considerable quantity on the mesentery, omentum, kidneys, &c.

Obs. The intermitting pulse should seem to have been owing to effusions of water in some of the cavities of the breast, as it disappeared on the removal of the waters.

(p. 147) *Case II*

Mrs. C—— of K——, Aet. 80. Orthopnoea, with sense of oppression about the proecordia. Unable to lie down in bed for some nights past. Anasarca of the lower extremities. Urine very scanty. Complaints of six weeks standing. Had taken *sal. diuret. c. ol. junip.*—*Calom. c. jalap, et gambog.*—*Et ol. junip. c. ol. Terebinth.* without effect.

Feb. 7 Infus. Digital. e. dr. iii. ad aq. ℥c. oz. viii. cochl. ii. qtis horis. Ordered to drink largely of *infus. baccar. junip.* The third dose produced great nausea which continued ten hours, during which time the urine made was about a quart. The next day her apothecary directed her to begin again with it. The second dose produced vomiting. During the next twenty hours she made two quarts of water, about four times as much as she drank.

From this time she took no more of the *infus. Digital.* but continued the *inf. bacc. junip.* until about *March 2d*, when all the swellings were gone down, her respiration perfectly free, and she herself quite restored to her former state of health. On the 29th she had an attack of jaundice which was some time after removed; since which she has enjoyed a good state of health, excepting that for some little time past her ancles have been slightly oedematous, which will I trust soon yield to strengthening medicines.

(p. 148) *Case III*

Mrs. M—— G——, Aet. 64. Has had sore legs for these thirty-four years past. Orthopnoea. Sense of oppression at the praecordia. Pulse intermitting. Legs anasarcous. Urine scanty, high-coloured.

Infus. Digital. c. dr. iss ad. aq. bull. oz. viii. cochl. ii. 4tis horis.

Took six doses, when nausea was excited. Urine a quart during the course of the night. The flow of urine continued, and complaints relieved. Sal. Mart. c. extr. gent. and afterwards with the addition of extr. cort. for which last ingredient she had a predilection, confirmed the cure.

On the same day the next year I was called in to her for a similar train of symptoms, excepting that the pulse was but just perceptibly irregular.

Infus. Digital. u. a. praescript.

The directions on the phial not being attended to, *two doses of it were given after a nausea had been excited*, which, with occasional vomitings, became exceedingly oppressive. A saline draught, given in Dr. Hulme's method, a draught *sal. c. c. gr. xi. c. conf. card. gr. x.* produced no immediate effect, but the nausea gradually abating, inf. bacc. junip. was ordered; but this appeared to augment it, (p. 149) and a great propensity to sleep coming on, I directed *sal. c. c. conf. card. aa gr. viii. 4tis horis*, which removed the unpleasant symptoms and *myrrh. c. sal. mart.* completed the cure. During the use of the above medicines, the urine was augmented, and the pulmonary complaints removed, even before the nausea left her; and the sores of her legs which were much inflamed before she began with the infus. Digital. in a day's time assumed a much healthier appearance, and on her other complaints going off, they shewed a greater tendency to heal than she had ever observed in them for twenty years before. This instance is a very pleasing confirmation of the experience of Hulfe and Dr. Baylies, and of the advantage to be derived from a medicine, which, while it helps to heal the ulcers, removes that from the constitution which often renders the healing of them improper.

In one case in which I ordered it, the infusion, instead of digesting three hours as I had directed, was suffered to stand upon the leaves all night. The consequence was that the first dose produced considerable nausea.

The two following cases, with which I have been favoured by a physician very justly eminent, convince me of the necessity

there is that every one who discovers a new medicine, or new virtues in an old one, should, in announcing such discoveries, publish to the world the exact manner in which he exhibits (p. 150) such medicines, with all the precautions necessary to obtain the promised success.

In these (says my correspondent) "the infusion was given in small doses, repeated every hour or two, till a nausea was raised, when it was omitted for a day or perhaps two, and then repeated in the same manner."

"An Ascites emptied by it, but filled again very speedily, though *its use was never discontinued*, and who afterwards found no salutary effects from it. Ended fatally."

"In an Anasarca it sometimes increased the quantity of urine, and abated the swelling, but which as often returned in as great a degree as before, though *the medicine was still given*, and always increased in quantity so as to excite nausea. Ended fatally."

"I have tried it in many other cases, but found very little difference in the success attending it."

May we not be allowed to conjecture that the inefficacy of *its continued use* is owing to its narcotic property gradually diminishing the irritability of the muscular fibres of the absorbents, or possibly of the whole vascular system, and thus adding to that weakened action which seems to be the cause of the general-ity of dropsies, which leads us to caution the medical experimenter against trying it, at least (p. 151) *against its continued use, even in small doses*, in other diseases of diminished energy, as continued fever, palsy, &c.

I remain with the greatest truth,

Your obliged and affectionate friend,

JONATHAN STOKES.

Stourbridge,
May 17, 1785.

THE three following Hospital Cases, which DR. STOKES had an opportunity of observing, are related as instances of bad practice, and tend to demonstrate how necessary it is when one physician adopts the medicine of another, that he should also at first rigidly adopt his method.

Case I

Esther K——, Aet. 33. General anasarca, ascites, and dyspnoea, of seven months duration.

Decoct. e Digit. dr. iv. c. aq. lb. i. coquend. ad. lb. ss. cap. oz. i. 2dis. horis. 1st Day. 4th dose made her sick. 2d Day. The first dose she took today produced vomiting.

(p. 152) 3d Day. *Minuatur dosis ad oz. ss.* This stayed upon her stomach, but produced an almost constant sickness. Stools more frequent, water scarce sensibly increased; and her swellings not at all reduced.

4th Day. *Cap. Calomel. gambog. scill. ℥c.*

OBS. Sufficient time was not allowed to observe its effects, neither was the patient enjoined the free use of diluents. The disease terminated fatally.

Case II

William T——, Aet. 42. Ascites, with cough and dyspnoea. Abdomen very much distended. The rest of his body highly emaciated. Urine thick, high coloured, and in very small quantity.

Decoct Digit. (u. in Esther K——.) 4tis horis.

1st Day of taking it. The 4th dose produced sickness.

2d. Vomiting after the second dose.

10th. Urine increased to lb. vi.

11th. Flow of urine continues. Abdomen quite flaccid.

(p. 153) 12th. Abdomen not diminished.

15th. A smart purging came on, and the flow of urine diminished.

23rd. Belly much bound. Took a cathart. powder, which was followed by a diminution of the abdomen.

29th. To take a cathart. powder every 4th morning, continuing the decoct. Digit.

32d. Urine exceedingly scanty.

35th. *Vin. scill. oz. ss. o. m. ℥c.* This produced diuretic effects.

44th. Tapped. Terminated fatally.

OBS. Here the medicine was *continued till it ceased to produce*

diuretic effects; and these effects were not aided by any strengthening remedies.

Case III

George R——, Aet. 52. Ascites, general anasarca, and dyspnoea. His legs so greatly distended that it was with great difficulty he could draw the one after the other.

(p. 154) *Infus. Digital. dr. iii ss. ad. aq. lb. ss. cap. oz. i. altern. horis donec nauseam excitaverit. Rep. 3 tiis diebus. tempore intermedio cap. sol. guaic. oz. i. ter in die ex inf. sinap.*

1st Day of taking it. Became sickish towards night.

2d Day. Made a great quantity of water during the night, and spat up a great deal of watery phlegm. The first dose he took in the morning has produced a sickness which has continued all day, but he has never vomited.

3d Day. The change in his appearance so great as to make it difficult to conceive him to be the same person. Instead of a large corpulent man, he appeared tall, thin, and rather aged. Breathes freely, and can walk up and down stairs without inconvenience.

4th Day. *Decoct. bacc. junip. and cyder for common drink.*

6th Day. A second course of his medicine produced a flow of urine almost as plentiful as the former, though he drank little or nothing at the time. In a day or two after he walked to some distance.

12th Day. *Pot. purgans illico.*

14th Day. *Pot. purg. c. jalap. dr. ss. 4tis diebus. Infus. Dig. 3tiis diebus.*

(p. 155) 17th Day. *R. Gamb. gr. iii. calom. gr. ii. camph. gr. i. syr. simpl. fiat pil. o. n. sum. Infus. Digit. 3 tiis diebus.*

21st Day. Made an out-patient. The superabundant flow of urine continued for the first three days after his last course; but since, the flow of saliva has been nearly equal to that of urine.

The smalls of his legs not quite reduced, and are fuller at night. He has shrunk round the middle from four feet two inches to

three feet six inches; and in the calves of his legs, from seventeen inches to thirteen and a half.*

Obs. The waters were here very successfully evacuated, but as you remarked to me, on communicating the case to you at the time, tonic medicines should have been given, to second the ground that had been gained, instead of weakening the patient by drastic purgatives.

(p. 156) A CASE from Mr. SHAW, Surgeon, at Stourbridge.—
Communicated by Doctor STOKES.

Matth. D—, Aet. 71. Tall and thin. Disease a general anasarca, with great difficulty of breathing. The lac ammoniac. somewhat relieved his breath; but the swellings increased, and his urine was not augmented. I considered it as a lost case, but having seen the good effects of the Digitalis, as ordered by Dr. Stokes in the case of Mrs. G—, I gave him one spoonful of an infusion of oz. ii. to half a pint, twice a day. His breath became much easier, his urine increased considerably, and the swellings gradually disappeared; since which his health has been pretty good, except that about three weeks ago, he had a slight dyspnoea, with pain in his stomach, which were soon removed by a repetition of the same medicine.

Mr. Shaw likewise informs me, that he has removed pains in the stomach and bowels, by giving a spoonful of the infusion, dr. iss. to oz. viii. morning and night.

(p. 157) A LETTER from Mr. VAUX, Surgeon, in Birmingham

DEAR SIR,

I SEND you the two following cases, wherein the Digitalis had very powerful and sensible effects, in the cure of the different patients.

* In the three last recited cases, the medicine was directed in doses quite too strong, and repeated too frequently. If Esther K— could have survived the extreme sickness, the diuretic effects would probably have taken place, and, from her time of life, I should have expected a recovery. Wm. T— seems to have been a bad case, and I think would not have been cured under any management. G. R— certainly possessed a good constitution, or he must have shared the fate of the other two.

Case I

Mrs. O—— of L—— Street, in this town, aged 28, naturally of a thin, spare habit, and her family inclinable to phthisis, sent for me on the 11th of June, 1779, at which time she complained of great pain in her side, a constant cough, expectorated much, which sunk in water; had colliquative sweats and frequent purging stools; the lower extremities and belly full of water, and from the great difficulty she had in breathing, I concluded there was water in the chest also. The quantity of water made at a time for three weeks before I saw her, never amounted to more than a tea-cup full, frequently not so much. Finding her in so alarming a situation, I gave it as my opinion she could receive no benefit from medicine, and requested her not to take any; but she being very desirous of my ordering her something, I complied, and sent her a box of gum pills with squills, and a mixture with salt of tartar: these medicines she took until the sixteenth, without any good effects: the water in her legs now began to exsude (p. 158) through the skin, and a small blister on one of her legs broke. Believing she could not exist much longer, unless an evacuation of the water could be procured; after fully informing her of her situation, and the uncertainty of her surviving the use of the medicine, I ventured to propose her taking the *Digitalis*, which she cheerfully agreed to. I accordingly sent her a pint mixture, made as under, of the fresh leaves of the *Digitalis*. Three drams infused in one pint of boiling water, when cold strained off, without pressing the leaves, and two ounces of the strong juniper water added to it: of this mixture she was ordered four table spoonfulls every third hour, till it either made her sick, purged her, or had a sensible effect on the kidneys. This mixture was sent on the seventeenth, and she began taking it at noon on the eighteenth. At one o'clock the following morning I was called up, and informed she was dying. I immediately attended her, and was agreeably surprised to find their fright arose from her having fainted, in consequence of the sudden loss of twelve quarts of water she had made in about two hours. I immediately applied a roller round her belly, and, as soon as they could be made, 2 others, which were carried from the toes quite up to

the thighs. The relief afforded by these was immediate; but the medicine now began to affect her stomach so much, that she kept nothing on it many minutes together. I ordered her to drink freely of beef tea, which she did, but kept it on her stomach but a very short time. A neutral draught in a state of effervescence was taken to no good purpose: She therefore continued (p. 159) the beef tea, and took no other medicine for five days, when her sickness went off: her cough abated, but the pain in her side still continuing, I applied a blister which had the desired effect: her urine after the first day flowed naturally. Her cure was completed by the gum pills with steel and the bitter infusion. It must be observed she never had any collection of water afterwards.

It affords me great pleasure to inform you that she is now living, and has since had four children; all of whom, I think I may justly say, are indebted to the *Digitalis* for their existence.

There appears in this case a striking proof of the utility of emetics in some kinds of consumptions, as it appears to me the dropsy was brought on by the cough, &c. and I believe these were cured by the continual vomitings, occasioned by the medicine.

Case II

Mr. H——, a publican, aged about 48 years, sent for me in *March*, 1778. He complained of a cough, shortness of breathing, which prevented him from laying down in bed; his belly, thighs and legs very much distended with water; the quantity of urine made at a time seldom exceeded a spoonful. I requested him to get some of the *Digitalis*, and as they had no proper weights in the house, I told them to put as much of the fresh leaves as would weigh down a guinea, into half a pint of boiling water; (p. 160) to let it stand till cold, then to pour off the clear liquor, and add a glass of gin to it, and to take three table spoonfuls every third hour, until it had some sensible effect upon him.

Before he had taken all the infusion, the quantity of urine made increased, (he therefore left off taking it), and it continued to do so until all the water was evacuated. His breathing became much better, his cough abated, though it never quite left him;

he being for some time before asthmatic. By taking some tonic pills he continued quite well until the next spring, when he had a return of his complaint, which was carried off by the same means. Two years after, he had a third attack, and this also gave way to the medicine. Last year he died of a pleurisy.

I am, &c.

Moor-Street, 8th May,

JER. VAUX.

1785.

P. S. You must well recollect the case of Mrs. F.—. —It was “a general dropsy—every time she took the medicine its effects were similar, viz. The discharge of urine came on gradually at first, increased afterwards, and the whole of the water both in the belly, legs, &c. was perfectly evacuated. Although the effects were only temporary, they were exceedingly agreeable to the patient, making her time much more comfortable.”—(*See Case XLIII.*)

(p. 161) A LETTER from MR. WAINWRIGHT, Surgeon, in
Dudley

DEAR SIR,

It gives me great pleasure to find you intend to publish your observations on the *Digitalis purpurea*.

Several years are now elapsed since you communicated to me the high opinion you entertained of the diuretic qualities of this noble plant. To ensure success, due attention was recommended to its *preparation*, its *dose*, and its *effects* upon the system.

I always gave the infusion of the dried leaves; the dose the same as in the prescriptions returned. If the medicine operated on the stomach or bowels, it was thought prudent to forbear. When the kidneys began to perform their proper functions, and the urine to be discharged, a continuance of its farther use was unnecessary.

These remarks you made in the case of the first patient for whom you prescribed the *Digitalis* in our neighbourhood, and I have found them all necessary at this present period. From the *decided* good effects that followed from its use, in those cases where the most powerful remedies had failed, I was soon convinced it was a most valuable addition to the *materia medica*.

(p. 162) The want of a certain diuretic, has long been one of the desiderata of medicine. The *Digitalis* is undoubtedly at the head of this class, and will seldom, if properly administered, disappoint the expectation. I can speak with the more confidence, having, in an extensive practice, been a happy witness to its good qualities.

For several years, I have given the infusion in a variety of cases, where there was a deficiency in the secretion of the urine, with the greatest success. In recent obstructions, I do not recollect many failures. In anasarctous diseases, and in the anasarca, when combined with the ascites; in swellings of the limbs, and in diseases of the chest, when there was the greatest reason to believe an accumulation of serum, the most beneficial consequences have followed from its use.

Had I been earlier acquainted with your intention to publish an account of the *Digitalis*, I could have transmitted some cases, which might have served to corroborate these assertions: but I am convinced the *Digitalis* needs not my assistance to procure a favorable reception. Its own merit will ensure success, more than a hundred recited cases.

I could wish those gentlemen who intend to make use of this plant, to collect it in a hot dry day, when the petals fall, and the seed-vessels begin to swell.

(p. 163) The leaves kept to the second year are weaker, and their diuretic qualities much diminished. It will therefore be necessary to gather the plant fresh every season.

These cautions are unnecessary to the accurate botanist, who well knows, that a plant in the spring, though more succulent and full of juices, is destitute of those qualities which may be expected when that plant has attained its full vigour, and the seed-vessels begin to be manifest. But for want of attention to these particulars, its virtues may be thought exaggerated, or doubtful, if beneficial consequences do not always flow from its use. There are diseases it cannot cure; and in several of those patients in this town, who first took the *Digitalis* by your orders, there was the most positive proof of the viscera being unsound. In these desperate cases it often procured a plentiful flow of urine, and palliated a disease which medicine could not remove.

At a remote distance, physicians are seldom applied to for advice in trifling disorders. Many remedies have been tried without relief, and the disease is generally obstinate or confirmed. —It would not be fair to try the merits of the *Digitalis* on this scale. It might often fail of promoting the end desired. I flatter myself the reputation of this plant will be equal to its merit, and that it will meet with a candid reception.

(p. 164) As there is no pleasure equal to relieving the miseries and distresses of our fellow-creatures, I hope you will long enjoy that peculiar felicity.

Permit me to return my thankful acknowledgments, for your free communication of a medicine, by which means, through the blessing of providence, I have been enabled to restore health and happiness to many miserable objects.

I am, &c.

Yours,

J. WAINWRIGHT.

Dudley, April 26th,
1785.

CASE of MR. WARD, Surgeon, in Birmingham.—Related by himself

IN *September*, 1782, I was seized with a difficulty of breathing, and oppression in my chest, in consequence of taking cold from being called out in the night. My tongue was foul; my urine small in quantity; my breath laborious and distressing on the slightest exercise. I tried the medicines most generally recommended, such as emetics, blisters, lac ammoniacum, oxymel of squills, &c. but finding little or no relief, I consulted Dr. Withering, who advised me to try the following prescription.

(p. 165) R. Sol. Digital. purp. siccat. dr. iss.

Aq. bullientis oz. iv.

Aq. cinn. sp. oz. ss. digere per horas quatuor, et colaturae capiat cochlear. i. nocte maneque.

He also desired me to take fifty drops of tincture of cantharides three or four times a day.

After taking eight ounces of the infusion, and about twelve

drams of the drops, I was perfectly cured, and have had no return since. The medicine did not occasion sickness or vertigo, nor had they any other sensible effect than in changing the appearance, and increasing the quantity of the urine, and rendering the tongue clean. After the last dose or two indeed, I had a little nausea, which was immediately removed by a small glass of brandy.

Birmingham, 1st July, 1785.

Communications from MR. YONGE, Surgeon, in Shiffnall,
Shropshire

DEAR SIR,

I HAVE great satisfaction in complying with your just claim, by transcribing outlines of the subsequent cases, for insertion in your long requested tract on the *Digitalis purpurea*. The two first of these you will easily recollect, the cures having been conducted immediately upon your own management, (p. 166) and the whole may add to that weight of evidence which long experience enables you to adduce to the efficacy of that valuable medicine. I have recited the only instances of its failure which occur to me, but many other, though successful cases, wherein its utility might seem dubious, and also the accounts received from people whose accuracy might be suspected, I shall not for obvious reasons trouble you with.

I am, dear Sir,

Your obliged friend,

WILLIAM YONGE.

Shiffnall,

May 1, 1785.

Case I

A Gentleman aged 49, on the night of the 21st of August, 1784, awaked with a sense of suffocation, which obliged him to rise up suddenly in bed. I found him complaining of difficult respiration, particularly on lying down; the countenance pale, and the pulse smaller and quicker than usual. Some brandy and water having been given, the symptoms gradually abated, so

that he slept in a half recumbent posture. The following day he expressed a sense of anxiety and weight in the chest, attended by quicker breathing upon motion of the body. That evening an emetic of ipecacohana was given, and afterwards a draught, with vitriolic aether (p. 167) and confect. card. aa dr. i. to be repeated as the symptoms should require it. He continued to be affected with slighter returns of the dyspnoea at irregular intervals, until *September 15th*, when upon a more severe attack, the emetic was repeated. He now recollected some slight pain in his arms which had affected him previous to this last seizure, and was disposed to consider his complaint as rheumatic. Pills with gum ammoniac. gum guaiac. and antimonial powder were directed, with infus. amar. simpl. twice a day. The bowels were regulated by aperient pills of pulv. jalap. aloes and sal. tartar. and dr. iss balsam peruv. was given occasionally to alleviate the paroxysms of dyspnoea.

From this period until the beginning of November, little amendment or variation happened, except that respiration became more permanently difficult, and particularly oppressed upon motion, nor was it relieved by the expectoration of a mucous discharge, which now increased considerably. Squills, musk, ol. succini, aether, with other medicines of the same kind, were now used, but without success. The effects of opium and venaesection were tried. The appetite diminished, and his sleep became short and disturbed. He sometimes slept lying upon his back, but generally upon his left side. The urine which had hitherto been of good colour, and sufficient quantity, now became diminished, and lateritious; and the ancles oedematous.

(p. 168) On the 15th of *November* a blister was laid over the sternum, and dr. iss. of oxymel scillitic. was given every eight hours.

On the 18th, a more copious discharge of urine took place; the swelling of the feet soon disappeared, and the respiration became gradually relieved.

On 30th dr. i. tinct. cantharidum twice a day in pyrmont water, with pills of ammoniac, sal tartar. et extract. gentian. were substituted, but

On the 7th of *December*, from some symptoms of relapse, the oxymel was used as before, and continued to be taken until the 27th, in doses as large as could be dispensed with on account of the great nausea which attended its exhibition: The urine was made in the quantity of four to five pints each day, during the whole time; the quantity then drank being seldom more than three pints. But now the sickness being exceedingly depressing, the strength failing, and the diuretic effects beginning to cease, the following prescription was directed.

R. Sol. Digitalis purpur. pulv. scruples ss.

Spec. Aromatic. scruples i. sp. lav. c. f. pilul. no. x. capiat i. nocte manequē, et alternis diebus sensim augeatur dosin.

In three days the effect of this medicine became visible, and when the dose of the Digitalis had been (p. 169) increased to six grains per day, the flow of urine generally amounted to seven pints every twenty-four hours. Not the least sickness, nor any other disagreeable symptom supervened, though he persevered in this plan until the end of *January* at which time the dyspnoea was removed, and he has continued gradually to regain his flesh, strength, and appetite, without any relapse.

Case II

About the middle of the year 1784 a lady aged 48, returned from London, to her native air in Shropshire, under symptoms of complicated disease. It was your opinion that the plethoric state, consequent to that period, when menstruation first begins to cease, had under various appearances, laid the foundation of that deplorable state which now presented itself. The skin was universally of a pale, leaden colour; her person much emaciated, and her strength so reduced, as to disable her from walking without support. The appetite fluctuating, the digestion impaired so much, that solids passed the intestines with little appearance of solution: She had generally eight or ten alvine evacuations every day, and without this number, febrile symptoms, attended with severe vertiginous affection, and vomiting regularly ensued. The stools were of a pale ash colour. The urine generally pale, and at first in due quantity. The region of the stomach (p. 170)

had a tense feel, without soreness: the feet and ancles oedematous, her sleep was uncertain: the pulse varying between 94 and 100 and feeble, except upon the approach of the menstrual periods, which were now only marked by its increased strength, and exacerbation of other febrile symptoms. Emetics, saline medicines, and gentle aperients were necessary to alleviate these. Six grains of ipecac operated with sufficient power, and half a grain of calomel would have purged with great violence.

From the time of her arrival till the middle of *August*, mercury had been continued in various forms, and in doses such as the irritable state of her stomach and bowels would admit of. Spirit. nitri dulc.; sal. tartar. squill, and cantharides were alternately employed as diuretics, but without success, to retard the progress of an universal anasarca, which was then advanced to such degree and accompanied by so great debility, and other dreadful concomitants, as to threaten a speedy and fatal catastrophe.

On the 16th of *August* you first saw her, and directed thus.

R. Mercur. cinerei gr. ii.

Sol Digital. purpur. pulv. scruples i. f. mass. in pill. no. xvi. dividend.—sumat unam hora meridiana, iterumque hora quinta pomeridiana quotidie.

(p. 171) Capiat lixivii saponac. gutt. L. in haust. juscul. sine sale parati omni nocte.

On the 20th the flow of urine began to increase, and she continued the medicine in the same dose until the 20th of *September*, discharging from six to eight pints of water each day for the first week, and which quantity gradually diminished as she became empty. During this period she complained not of any sickness, except from the lixivium, which was after the first dose reduced to 20 drops; and her appetite and strength increased daily, though it was evident that no bile had yet flowed into the bowels, nor was the digestion at all improved. The anasarcaous appearances being then removed, the Digitalis was omitted, and pills, composed of mercur. cinereus, aloes, and sal tartari directed twice a day, with dr. i. of vin. chalybeat. in infus. amar. simpl.

Her amendment in other respects proceeded slowly, but regularly, from that time until the 9th of October; when the state

of plethora again recurring, with its usual attendant symptoms, oz. iv. of blood were taken from the arm; and this was upon the same occasion, repeated in the following month, with manifest good consequences; though in both instances the colour of the blood, as flowing from the vein could hardly be called red, and the coagulum was as weak in its cohesion as possible. The state of the stomach and bowels was by this time greatly improved, in common with other parts of (p. 172) the system; but no introduction of bile had yet happened: the hardness about the hypogastric region, though less, continued in a considerable degree, and you ordered pills of mercury rubbed down, and rust of iron, to be taken twice a day, with a decoction of dandelion and sal sodae.

A cataplasm of linseed was applied every night over the stomach and right side; and, with little deviation from this plan, she continued to the end of the year, improving in her general health, but the hepatic affection yet remaining. It was then determined to try the effects of electricity, and gentle shocks were passed through the body daily, and as nearly as could be through the liver, in various directions.

On the fifth day there was reason to think that some gall had been secreted and poured out, and this became every day more evident; but it flowed only in small quantity, and irregularly into the bowels, as appeared from the faeces being partially tinged by it.

In *February* the lady left this neighbourhood, and though convalescent, yet so nearly well as to promise us the satisfaction of seeing her perfectly restored.

June 29. The bile is now secreted in pretty good quantity, her appetite is perfectly good, her strength equal to almost any degree of exercise, and her (p. 173) health in general better than it has been for some years.

Case III

Mr. W—, aged —. In *June*, 1782, was affected with slight difficulty in respiration, upon taking exercise or lying down in bed. These symptoms increased gradually until the end of

July, when he complained of sense of weight and uneasiness about the proecordia; loss of appetite; and costiveness. The urine was small in quantity, and high coloured; his pulse feeble, and intermitting; he breathed with difficulty when in bed, and slept little. After the exhibition of an emetic, and an opening medicine of rhubarb, sena, and sal tartari, he was directed to take half a dram of squill pill, pharm. Edinburg. night and morning, with dr. ss sal. sodae in oz. iss. infus. amar. simpl. twice a day; and these medicines were continued during ten days, without any sensible effect. A blister was then applied to the sternum, and six grains of calomel given in the evening. The symptoms were now increased very considerably, in every particular; and the following infusion was substituted for the former medicines.

R. Fol. Digital. purpur. dr. iii.

Cort. limon. dr. ii. infund.

Aq. bullient. lb. i. per hor. 2 et cola. sumat cochl. i. promane et repet. omni hora.

(p. 174) Sometime in the night considerable nausea occurred, and the following day he began to make water in great quantity, which he continued to do for three or four days. The pulse in a few hours became regular, slower, and stronger, and, in the course of a week, all the symptoms entirely vanished, and an electuary of cort. peruvian, sal martis, and spec. aromatic. confirmed his cure.

In *February*, 1784, this gentleman had a relapse of his disease, from which he again soon recovered by the same means, and is now perfectly well.

Case IV

G—A—, a husbandman, aged 57. Was in the year 1782 affected with a slight, but constant pain in his breast, with difficult respiration. His countenance was yellow; the abdomen swelled, and hard; his urine high coloured, and in small quantity; appetite and sleep little. Complained of frequent nausea and of sudden profuse sweatings, which seemed for a short time to relieve the dyspnoea.

After the exhibition of an emetic, six grains of calomel were given, with a purge of jalap in the morning, and repeated in a few days, with some appearance of advantage. He was then directed to take some pills of squill, soap, and rhubarb, with a draught twice a day, consisting of *infus. amar. simp. and sal tartari*. The skin soon became clearer and (p. 175) the pain in his breast considerably diminished. But every other circumstance remaining the same, and a fluctuation in the belly being now more evident, the infusion of *digitalis* as prescribed in case third, was given in the dose of one ounce twice a day.

On the 5th day the effects were apparent, and he continued his medicine for a fortnight without nausea, making four or five pints of water every night, but little in the day, and gradually losing the symptoms of his disease.

In 1784, this person had a relapse, and was again cured by similar treatment.

Case V

R—— H——, Aged 43. Towards the end of the year 1783, became affected with slight cough and expectoration of purulent matter. In December his skin became universally of a pale yellow colour. The abdomen was swelled and hard; his appetite little, and he complained of a violent and constant palpitation of the heart, which prevented him from sleeping. The urine pale, and in small quantity. The pulse exceedingly strong, and rebounding; beating 114 to 120 strokes every minute. He suffered violent pain of his head, and was very feeble and emaciated. After bleeding, and the use of gentle aperient medicines, he continued to take the infusion of *Digitalis* for some days, without any sensible effect. Other diuretics were tried to as little purpose (p. 176). Repeated bleeding had no effect in diminishing the violent action of the heart. He died in January following, under complicated symptoms of phthisis and ascites.

Case VI

A man aged 57, who had lived freely in the summer of 1784, became affected with oedematous swelling of his legs, for which

he was advised to drink Fox Glove Tea. He took a four ounce bason of the infusion made strong with the green leaves, every morning for four successive days.

On the 5th he was suddenly seized with faintness and cold sweatings. I found him with a pale countenance, complaining of weakness, and of pain, with a sense of great heat in his stomach and bowels. The swelling of the legs was entirely gone, he having evacuated urine in very large quantities for the two preceding days. He was affected with frequent diarrhoea. The pulse was very quick and small, and his extremities cold.

A small quantity of broth was directed to be given him every half hour, and blisters were applied to the ancles, by which his symptoms became gradually alleviated, and he recovered perfectly in the space of three weeks; except a relapse of the anasarca, for which the *Digitalis* was afterwards successfully employed, in small doses, without any disagreeable consequence.

(p. 177) *Case VII*

S—D—, a middle aged single woman, was affected in the year eighty-one, with a painful rigidity and slight inflammation of the integuments on the left side, extending from the ear to the shoulder. In every other particular she was healthy. The use of warm fomentations, and opium, with two or three doses of mercurial physic, afforded her ease and the inflammation disappeared, but was succeeded by an oedematous swelling of the part, which very gradually extended along the arm, and downward to the breast, back, and belly. Friction, electricity and mercurial ointment were amongst the number of applications unsuccessfully employed to relieve her for the space of three months, during which time she continued in good general health.

In *November* she became ascitic, passing small quantities of urine, and soon afterwards a sudden dyspnoea gave occasion to suppose an effusion of water in the thorax. The *Digitalis*, squills, and cantharides were given in very considerable doses without effect. She died the latter end of December following.

Case VIII

W—— C——, a collier aged 58, was attacked in the spring of 1783 with tertian ague, which he attributed to cold, by sleeping in a coal (p. 178) pit, and from which he recovered in a few days, except a swelling of the lower extremities, which had appeared about that time, and gradually increased for two or three months. The legs and thighs were greatly enlarged and oedematous. His belly was swelled, but no fluctuation perceptible. He made small quantities of high coloured water. The appetite bad, and pulse feeble. He had taken many medicines without relief, and was now so reduced in strength, as to sit up with difficulty. An infusion of the *Digitalis* was directed for him, in the proportion of one ounce of the fresh leaves to a pint of water, two ounces to be taken three times a day, until the stomach or bowels became affected. Upon the exhibition of the sixth dose, nausea supervened, and continued to oppress him at intervals for two or three days, during which he passed large quantities of pale urine. The swelling, assisted by moderate bandage rapidly diminished, and without any repetition of his medicine, at the expiration of sixteen days, he returned to his labour perfectly recovered.

(p. 179) OF THE PREPARATIONS AND DOSES, OF THE FOXGLOVE

Every part of the plant has more or less of the same bitter taste, varying, however, as to strength, and changing with the age of the plant and the season of the year.

Root.—This varies greatly with the age of the plant. When the stem has shot up for flowering, which it does the second year of its growth, the root becomes dry, nearly tasteless, and inert.

Some practitioners, who have used the root, and been so happy as to cure their patients without exciting sickness, have been pleased to communicate the circumstance to me as an improvement in the use of the plant. I have no doubt of the truth of their remarks, and I thank them. But the case of Dr. Cawley puts this matter beyond dispute. The fact is, they have fortunately happened to use the root in its approach to its inert state, and consequently have not over dosed their patients. I could,

(p. 180) if necessary, bring other proof to shew that the root is just as capable as the leaves, of exciting nausea.

STEM.—The stem has more taste than the root has, in the season the stem shoots out, and less taste than the leaves. I do not know that it has been particularly selected for use.

LEAVES.—These vary greatly in their efficacy at different seasons of the year, and, perhaps, at different stages of their growth; but I am not certain that this variation keeps pace with the greater or lesser intensity of their bitter taste.

Some who have been habituated to the use of the recent leaves, tell me, that they answer their purpose at every season of the year; and I believe them, notwithstanding I myself have found very great variations in this respect. The solution of this difficulty is obvious. They have used the leaves in such large proportion, that the doses have been sufficient, or more than sufficient, even in their most inefficacious state. *The Leaf-stalks* seem, in their sensible properties, to partake of an intermediate state between the leaves and the stem.

FLOWERS.—The petals, the chives, and the pointal have nearly the taste of the leaves, and it has been suggested to me, by a very sensible and judicious friend, that it might be well to fix on the flower for internal use. I see no objection to the proposition, but I have not tried it.

(p. 181) SEEDS.—These I believe are equally untried.

From this view of the different parts of the plant, it is sufficiently obvious why I still continue to prefer the leaves.

These should be gathered after the flowering stem has shot up, and about the time that the blossoms are coming forth.

The leaf-stalk and mid-rib of the leaves should be rejected, and the remaining part should be dried, either in the sun-shine, or on a tin pan or pewter dish before a fire.

If well dried, they readily rub down to a beautiful green powder, which weighs something less than one-fifth of the original weight of the leaves. Care must be taken that the leaves be not scorched in drying, and they should not be dried more than what is requisite to allow of their being readily reduced to powder.

I give to adults, from one to three grains of this powder twice a

day. In the reduced state in which physicians generally find dropsical patients, four grains a day are sufficient. I sometimes give the powder alone; sometimes unite it with aromatics, and sometimes form it into pills with a sufficient quantity of soap or gum ammoniac.

If a liquid medicine be preferred, I order a dram of these dried leaves to be infused for four hours in half a pint of boiling water, adding to the strained liquor an ounce of any spirituous water. One ounce of this infusion given twice a day, is a medium dose for an adult patient. If the patient be stronger than usual, or the symptoms very urgent, this dose may be given once in eight hours; and on the contrary in many instances half an ounce at a time will be quite sufficient. About thirty grains of the powder or eight ounces of the infusion, may generally be taken before the nausea commences.

The ingenuity of man has ever been fond of exerting itself to vary the forms and combinations of medicines. Hence we have spirituous, vinous, and acetous tinctures; extracts hard and soft, syrups with sugar or honey, &c. but the more we multiply the forms of any medicine, the longer we shall be in ascertaining its real dose. I have no lasting objection however to any of these formulæ except the extract, which, from the nature of its preparation must ever be uncertain in its effects; and a medicine whose fullest dose in substance does not exceed three grains, cannot be supposed to stand in need of condensation.

It appears from several of the cases, that when the *Digitalis* is disposed to purge, opium may be joined with it advantageously; and when the bowels are too tardy, jalap may be given at the same time, (p. 183) without interfering with its diuretic effects; but I have not found benefit from any other adjunct.

From this view of the doses in which the *Digitalis* really ought to be exhibited, and from the evidence of many of the cases, in which it appears to have been given in quantities six, eight, ten or even twelve times more than necessary, we must admit as an inference either that this medicine is perfectly safe when given as I advise, or that the medicines in daily use are highly dangerous.

(p. 184) EFFECTS, RULES, AND CAUTIONS

The Foxglove when given in very large and quickly-repeated doses, occasions sickness, vomiting, purging, giddiness, confused vision, objects appearing green or yellow; increased secretion of urine, with frequent motions to part with it, and sometimes inability to retain it; slow pulse, even as slow as 35 in a minute, cold sweats, convulsions, syncope, death.*

When given in a less violent manner, it produces most of these effects in a lower degree; and it is curious to observe, that the sickness, with a certain dose of the medicine, does not take place for many hours after its exhibition has been discontinued; that the flow of urine will often precede, sometimes accompany, frequently follow the sickness at the distance of some days, and not unfrequently be checked by it. The sickness thus excited, is extremely different from that occasioned by any other medicine; it is peculiarly distressing to the patient; it ceases, it recurs again as violent as before; and thus it will continue to recur for three or four days, at distant and more distant intervals.

(p. 185) These sufferings of the patient are generally rewarded by a return of appetite, much greater than what existed before taking the medicine.

But these sufferings are not at all necessary; they are the effects of our inexperience, and would in similar circumstances, more or less attend the exhibition of almost every active and powerful medicine we use.

Perhaps the reader will better understand how it ought to be given, from the following detail of my own improvement, than from precepts peremptorily delivered, and their source veiled in obscurity.

At first I thought it necessary *to bring on and continue the sickness, in order to ensure the diuretic effects.*

I soon learnt that the nausea being once excited, it was unnecessary to repeat the medicine, as it was certain to recur frequently, at intervals more or less distant.

* I am doubtful whether it does not sometimes excite a copious flow of saliva.—See cases at pages 115, 154, and 155.

Therefore my patients were ordered *to persist until the nausea came on, and then to stop*. But it soon appeared that the diuretic effects would often take place first, and sometimes be checked when the sickness or a purging supervened.

(p. 186) The direction was therefore enlarged thus—*Continue the medicine until the urine flows, or sickness or purging take place*.

I found myself safe under this regulation for two or three years; but at length cases occurred in which the pulse would be retarded to an alarming degree, without any other preceding effect.

The directions therefore required an additional attention to the state of the pulse, and it was moreover of consequence not to repeat the doses too quickly, but to allow sufficient time for the effects of each to take place, as it was found very possible to pour in an injurious quantity of the medicine, before any of the signals for forbearance appeared.

Let the medicine therefore be given in the doses, and at the intervals mentionea above:—let it be continued until it either acts on the kidneys, the stomach, the pulse, or the bowels; let it be stopped upon the first appearance of any one of these effects, and I will maintain that the patient will not suffer from its exhibition, nor the practitioner be disappointed in any reasonable expectation.

If it purges, it seldom succeeds well.

The patients should be enjoined to drink very freely during its operation. I mean, they should drink whatever they prefer, and in as great quantity (p. 187) as their appetite for drink demands. This direction is the more necessary, as they are very generally prepossessed with an idea of drying up a dropsy, by abstinence from liquids, and fear to add to the disease, by indulging their inclination to drink.

In cases of ascites and anasarca; when the patients are weak, and the evacuation of the water rapid; the use of proper bandage is indispensably necessary to their safety.

If the water should not be wholly evacuated, it is best to allow an interval of several days before the medicine be repeated, that food and tonics may be administered; but truth compels me to say, that the usual tonic medicines have in these cases very often deceived my expectations.

From some cases which have occurred in the course of the present year, I am disposed to believe that the *Digitalis* may be given in small doses, viz. two or three grains a day, so as gradually to remove a dropsy, without any other than mild diuretic effects, and without any interruption to its use until the cure be completed.

If inadvertently the doses of the Foxglove should be prescribed too largely, exhibited too rapidly, or urged to too great a length; the knowledge of a remedy to counteract its effects would be a desirable (p. 188) thing. Such a remedy may perhaps in time be discovered. The usual cordials and volatiles are generally rejected from the stomach; aromatics and strong bitters are longer retained; brandy will sometimes remove the sickness when only slight; I have sometimes thought small doses of opium useful, but I am more confident of the advantage of blisters. Mr. Jones (*Page* 135) in one case, found mint tea to be retained longer than other things.

(p. 189) CONSTITUTION OF PATIENTS

Independent of the degree of disease, or of the strength or age of the patient, I have had occasion to remark, that there are certain constitutions favourable, and others unfavourable to the success of the *Digitalis*.

From large experience, and attentive observation, I am pretty well enabled to decide *a priori* on this matter, and I wish to enable others to do the same: but I feel myself hardly equal to the undertaking. The following hints, however, aiding a degree of experience in others, may lead them to accomplish what I yet can describe but imperfectly.

It seldom succeeds in men of great natural strength, of tense fibre, of warm skin, of florid complexion, or in those with a tight and cordy pulse.

If the belly in ascites be tense, hard, and circumscribed, or the limbs in anasarca solid and resisting, we have but little to hope.

On the contrary, if the pulse be feeble or intermitting, the countenance pale, the lips livid, the skin cold, the swollen belly soft and fluctuating, or (p. 190) the anasarcaous limbs readily

pitting under the pressure of the finger, we may expect the diuretic effects to follow in a kindly manner.

In cases which foil every attempt at relief, I have been aiming, for some time past, to make such a change in the constitution of the patient, as might give a chance of success to the *Digitalis*.

By blood-letting, by neutral salts, by chrystals of tartar, squills, and occasional purging, I have succeeded, though imperfectly. Next to the use of the lancet, I think nothing lowers the tone of the system more effectually than the squill, and consequently it will always be proper, in such cases, to use the squill; for if that fail in its desired effect, it is one of the best preparatives to the adoption of the *Digitalis*.

A tendency to paralytic affections, or a stroke of the palsy having actually taken place, is no objection to the use of the *Digitalis*; neither does a stone existing in the bladder forbid its use. Theoretical ideas of sedative effects in the former, and apprehensions of its excitement of the urinary organs in the latter case, might operate so as to make us withhold relief from the patient; but experience tells me, that such apprehensions are groundless.

(p. 191) INFERENCES

To prevent any improper influence, which the above recitals of the efficacy of the medicine, aided by the novelty of the subject, may have upon the minds of the younger part of my readers, in raising their expectations to too high a pitch, I beg leave to deduce a few inferences, which I apprehend the facts will fairly support.

- I. That the *Digitalis* will not universally act as a diuretic.
- II. That it does do so more generally than any other medicine.
- III. That it will often produce this effect after every other probable method has been fruitlessly tried.
- IV. That if this fails, there is but little chance of any other medicine succeeding.
- V. That in proper doses, and under the management now pointed out, it is mild in its operation, and gives less disturbance to the system, than squill, or almost any other active medicine.

VI. That when dropsy is attended by palsy, unsound viscera, great debility, or other complication of disease, neither the Digitalis, nor any other diuretic (p. 192) can do more than obtain a truce to the urgency of the symptoms; unless by gaining time, it may afford opportunity for other medicines to combat and subdue the original disease.

VII. That the Digitalis may be used with advantage in every species of dropsy, except the encysted.

VIII. That it may be made subservient to the cure of diseases, unconnected with dropsy.

IX. That it has a power over the motion of the heart, to a degree yet unobserved in any other medicine, and that this power may be converted to salutary ends.

(p. 193) PRACTICAL REMARKS ON DROPSY AND SOME OTHER
DISEASES

The following remarks consist partly of matter of fact, and partly of opinion. The former will be permanent; the latter must vary with the detection of error, or the improvement of knowledge. I hazard them with diffidence, and hope they will be examined with candour; not by a contrast with other opinions, but by an attentive comparison with the phenomena of disease.

Anasarca

1. THE anasarca is generally curable when seated in the subcutaneous cellular membrane, or in the substance of the lungs.

2. When the abdominal viscera in general are greatly enlarged, which they sometimes are, without effused fluid in the cavity of the abdomen; the disease is incurable. After death, the more solid viscera are found very large and pale. If the cavity contains water, that water may be removed by diuretics.

(p. 194) 3. In swollen legs and thighs, where the resistance to pressure is considerable, the tendency to transparency in the skin not obvious, and where the alteration of posture occasions but little alteration in the state of distension, the cure cannot be effected by diuretics.

Is this difficulty of cure occasioned by spissitude in the effused

fluids, by want of proper communication from cell to cell, or is the disease rather caused by a morbid growth of the solids, than by an accumulation of fluid?

Is not this disease in the limbs similar to that of the viscera (2)?

4. Anasarca swellings often take place in palsied limbs, in arms as well as legs; so that the swelling does not depend merely upon position.

5. Is there not cause to suspect that many dropsies originate from paralytic affections of the lymphatic absorbents? And if so, is it not probable that the *Digitalis*, which is so effectual in removing dropsy, may also be used advantageously in some kinds of palsy?

Ascites

6. If existing alone, (*i.e.*) without accompanying anasarca, is in children curable; in adults generally incurable by medicines. Tapping may be (p. 195) used here with better chance for success than in more complicated dropsies. Sometimes cured by vomiting.

Ascites and anasarca

7. INCURABLE if dependent upon irremediably diseased viscera, or on a gouty constitution, so debilitated, that the gouty paroxysms no longer continue to be formed.

In every other situation the disease yields to diuretics and tonics.

Ascites, anasarca, and hydrothorax

8. UNDER this complication, though the symptoms admit of relief, the restoration of the constitution can hardly be hoped for.

Asthma

9. THE true spasmodic asthma, a rare disease—is not relieved by *Digitalis*.

10. In the greater part of what are called asthmatical cases, the real disease is anasarca of the lungs, and is generally cured by diuretics. (See 1.) This is almost always combined with some swelling of the legs.

(p. 196) 11. There is another kind of asthma, in which change of posture does not much affect the patient. I believe it to be caused by an infarction of the lungs. It is incurable by diuretics; but it is often accompanied with a degree of anasarca, and so far it admits of relief.

Is not this disease similar to that in the limbs at (3.) and also to that of the abdominal viscera at (2.)?

Asthma and anasarca

12. IF the asthma be of the kind mentioned at (9 and 11,) diuretics can only remove the accompanying anasarca. But if the affection of the breath depends also upon cellular effusion, as it mostly does, the patient may be taught to expect a recovery.

Asthma and ascites

13. A RARE combination, but not incurable if the abdominal viscera are sound. The asthma is here most probably of the anasarcous kind (10;) and this being seldom confined to the lungs only, the disease generally appears in the following form.

(p. 197) *Asthma, ascites, and anasarca*

14. THE curability of this combination will depend upon the circumstances mentioned in the preceding section, taking also into the account the strength or weakness of the patient.

Epilepsy

15. IN epilepsy dependant upon effusion, the Digitalis will effect a cure; and in the cases alluded to, the dropsical symptoms are unequivocal. It has not had a sufficient trial in my hands, to determine what it can do in other kinds of epilepsy.

Hydatid dropsy

16. THIS may be distinguished from common ascites, by the want of evident fluctuation. It is common to both sexes. It does not admit of a cure either by tapping or by medicine.

Hydrocephalus

17. THIS disease, which has of late so much attracted the attention of the medical world, I believe, originates in inflammation; and that the water found in the ventricles of the brain after death, is the consequence, and not the cause of the illness.

It has seldom happened to me to be called upon in the earlier stages of this complaint, and the symptoms (p. 198) are at first so similar to those usually attendant upon dentition and worms, that it is very difficult to pronounce decidedly upon the real nature of the disease; and it is rather from the failure of the usual modes of relief, than from any other more decided observation, that we at length dare to give it a name.

At first, the febrile symptoms are sometimes so unsteady, that I have known them mistaken for the symptoms of an intermittent, and the cure attempted by the bark.

In the more advanced stages, the diagnostics obtrude themselves upon our notice, and put the situation of the patient beyond a doubt. But this does not always happen. The variations of the pulse, so accurately described by the late Dr. Whytt, do not always ensue. The dilatation of the pupils, the squinting, and the aversion to light, do not universally exist. The screaming upon raising the head from the pillow or the lap, and the flushing of the cheeks, I once considered as affording indubitable marks of the disease; but in a child which I sometime since attended with Dr. Ash, the pulse was uniformly about 85, (except during the first week, before we had the care of the patient). The child never shewed any aversion to the light; never had dilated pupils, never squinted, never screamed when raised from the lap or taken out of the bed, nor did we observe any remarkable flushing of the cheeks; and the sleep was quiet, but sometimes moaning.

(p. 199) Frequent vomiting existed from the first, but ceased for several days towards the conclusion. One or two worms came away during the illness, and it was all along difficult to purge the child. Three days before death, the right side became slightly paralytic, and the pupil of that eye somewhat dilated.

After death, about two ounces and a half of water were found in the ventricles of the brain, and the vessels of the dura mater were turgid with blood.

If I am right as to the nature of hydrocephalus, that it is at first dependant upon inflammation, or congestion; and that the water in the ventricles is a consequence, and not a cause of the disease; the curative intentions ought to be extremely different in the first and the last stages.

It happens very rarely that I am called to patients at the beginning, but in two instances wherein I was called at first, the patients were cured by repeated topical bleedings, vomits, and purges.

Some years ago I mentioned these opinions, and the success of the practice resulting from them, to Dr. Quin, now physician at Dublin. That gentleman had lately taken his degree, and had chosen hydrocephalus for the subject of his thesis in the year 1779. In this very ingenious essay, which he gave me the same morning, I was much pleased to find that the author had not only held the same (p. 200) ideas relative to the nature of the disease, but had also confirmed them by dissections.

In the year 1781, another case in the first stage demanded my attention. The reader is referred back to Case LXIX for the particulars.

I have not yet been able to determine whether the Digitalis can or cannot be used with advantage in the second stage of the hydrocephalus. In case XXXIII. the symptoms of death were at hand; in Case LXIX. the practice, though successful, was too complicated, and in Case CLI. the medicine was certainly stopped too soon.

When we consider what enormous quantities of mercury may be used in this complaint, without affecting the salivary glands, it seems probable that other parts may be equally insensible to the action of their peculiar stimuli, and therefore that the Digitalis ought to be given in much larger doses in this, than in other diseases.

Hydrothorax

18. UNDER this name I also include the dropsy of the pericardium.

The intermitting pulse, and pain in the arms, sufficiently distinguish this disease from asthma, and from anasarcaous lungs.

It is very universally cured by the Digitalis.

(p. 201) 19. I lately met with two cases which had been considered and treated as angina pectoris. They both appeared to me to be cases of hydrothorax. One subject was a clergyman, whose strength had been so compleatly exhausted by the continuance of the disease, and the attempts to relieve it, that he did not survive many days. The other was a lady, whose time of life made me suspect effusion. I directed her to take small doses of the pulv. Digitalis, which in eight days removed all her complaints. This happened six months ago, and she remains perfectly well.

Hydrothorax and anasarca

20. THIS combination is very frequent, and, I believe, may always be cured by the Digitalis.

21. Dropsies in the chest either with or without anasarcaous limbs, are much more curable than those of the belly. Probably because the abdominal viscera are more frequently diseased in the latter than in the former cases.

Insanity

22. I APPREHEND this disease to be more frequently connected with serous effusion than has been commonly imagined.

23. Where appearances of anasarca point out the true cause of the complaint, as in cases XXIV. and (p. 202) XXXIV. the happiest effects may be expected from the Digitalis; and men of more experience than myself in cases of insanity, will probably employ it successfully in other less obvious circumstances.

Nephritis calculosa

24. WE have had sufficient evidence of the efficacy of the Foxglove in removing the Dysuria and other symptoms of this

disease; but probably it is not in these cases preferable to the tobacco.*

Ovarium dropsy

25. THIS species of encysted dropsy is not without difficulty distinguishable from an ascites; and yet it is necessary to distinguish them, because the two diseases require different treatment and because the probability of a cure is much greater in one than in the other.

26. The ovarium dropsy is generally slow in its progress; for a considerable time the patient though somewhat emaciated, does not lose the appearance of health, and the urine flows in the usual quantity. It is seldom that the practitioner is called in early enough to distinguish by the feel on which side the cyst originated, and the patients do not attend to that circumstance themselves. They generally menstruate (p. 203) regularly in the incipient state of the disease, and it is not until the pressure from the sac becomes very great, that the urinary secretion diminishes. In this species of dropsy, the patients, upon being questioned, acknowledge even from a pretty early date, pains in the upper and inner parts of the thighs, similar to those which women experience in a state of pregnancy. These pains are for a length of time greater in one thigh than in the other, and I believe it will be found that the disease originated on that side.

27. The ovarium dropsy defies the power of medicine. It admits of relief, and sometimes of a cure, by tapping. I submit to the consideration of practitioners, how far we may hope to cure this disease by a seton or a caustic.—In the LXIst case the patient was too much reduced, and the disease too far advanced to allow of a cure by any method; but it teaches us that a caustic may be used with safety.

28. When tapping becomes necessary, I always advise the adoption of the waistcoat bandage or belt, invented by the late very justly celebrated Dr. Monro, and described in the first volume of the Medical Essays. I also enjoin my patients to wear this bandage afterwards, from a persuasion that it retards

* See an original and valuable treatise by Dr. Fowler, entitled, *Medical Reports of the Effects of Tobacco*.

the return of the disease. The proper use of bandage, when the disorder first discovers itself, certainly contributes much to prevent its increase.

(p. 204) *Ovarium dropsy with anasarca*

29. THE anasarca does not appear until the encysted dropsy is very far advanced. It is then probably caused by weakness and pressure. The Digitalis removes it for a time.

Phthisis pulmonalis

30. This is a very increasing malady in the present day. It is no longer limited to the middle part of life: children at five years of age die of it, and old people at sixty or seventy. It is not confined to the flat-chested, the fair skinned, the blue eyed, the light-haired, or the scrophulous: it often attacks people with full chests, brown skins, dark hair and eyes, and those in whose family no scrophulous taint can be traced. It is certainly infectious. The very strict laws still existing in Italy to prevent the infection from consumptive patients, were probably not enacted originally without a sufficient cause. We seem to be approaching to that state which first made such restrictions necessary, and in the further course of time, the disease will probably fall off again, both in virulency and frequency.

31. The younger part of the female sex are liable to a disease very much resembling a true consumption, and from which it is difficult to distinguish it; but this disease is curable by steel and bitters. A criterion of true phthisis has been sought for in the (p. 205) state of the teeth; but the exceptions to that rule are numerous. An unusual dilatation of the pupil of the eye, is the most certain characteristic.*

32. Sydenham asserts, that the bark did not more certainly

* Many years ago I communicated to my friend, Dr. Percival, an account of some trials of breathing fixed air in consumptive cases. The results were published by him in the second Vol. of his very usefull Essays Medical and Experimental, and have since been copied into other publications. I take this opportunity of acknowledging that I suspect myself to have been mistaken in the nature of the disease there mentioned to have been cured. I believe it was a case of *Vomica*, and not a true *Phthisis* that was cured. The *Vomica* is almost always curable. The fixed air corrects the smell of the matter, and very shortly removes the hectic fever. My patients not only inspire it, but I keep large jars of the effervescing mixture constantly at work in their chambers.

cure an intermittent, than riding did a consumption. We must not deny the truth of an assertion, from such authority, but we must conclude that the disease was more easily curable a century ago than it is at present.

33. If the *Digitalis* is no longer useful in consumptive cases, it must be that I know not how to manage it, or that the disease is more fatal than formerly; for it would be hard to deny the testimony cited at page 9. I wish others would undertake the enquiry.

34. When phthisis is accompanied with anasarca, or when there is reason to suspect hydrothorax, the *Digitalis* will often relieve the sufferings, and prolong the life of the patient.

(p. 206) 35. Many years ago, during an attendance upon Mr. B——, of a consumptive family, and himself in the last stage of a phthisis; after he was so ill as to be confined to his chamber, his breathing became so extremely difficult and distressing, that he wished rather to die than to live, and urged me warmly to devise some mode to relieve him. Suspecting serous effusion to be the cause of this symptom, and he being a man of sense and resolution, I fully explained my ideas to him, and told him what kind of operation might afford him a chance of relief; for I was then but little acquainted with the *Digitalis*. He was earnest for the operation to be tried, and with the assistance of Mr. Parrott, a very respectable surgeon of this place, I got an opening made between the ribs upon the lower and hinder part of the thorax. About a pint of fluid was immediately discharged, and his breath became easy. This fluid coagulated by heat.

After some days a copious purulent discharge issued from the opening, his cough became less troublesome, his expectoration less copious, his appetite and strength returned, he got abroad, and the wound, which became very troublesome, was allowed to heal.

He then undertook a journey to London; whilst there he became worse: returned home, and died consumptive some weeks afterwards.

(p. 207) *Puerperal anasarca*

36. THIS disease admits of an easy and certain cure by the Digitalis.

37. This species of dropsy may originate from other causes than child birth. In the beginning of last *March*, a gentleman at Wolverhampton desired my advice for very large and painful swelled legs and thighs. He was a temperate man, not of a drop-sical habit, had great pain in his groins, and attributed his complaints to a fall from his horse. He had taken diuretics, and the strongest drastic purgatives with very little benefit. Considering the anasarca as caused by the diseased inguinal glands, I ordered common poultice and mercurial ointment to the groins, three grains of pulv. sol. Digitalis night and morning, and a cooling diuretic decoction in the day-time. He soon lost his pain, and the swellings gradually subsided.

THE END

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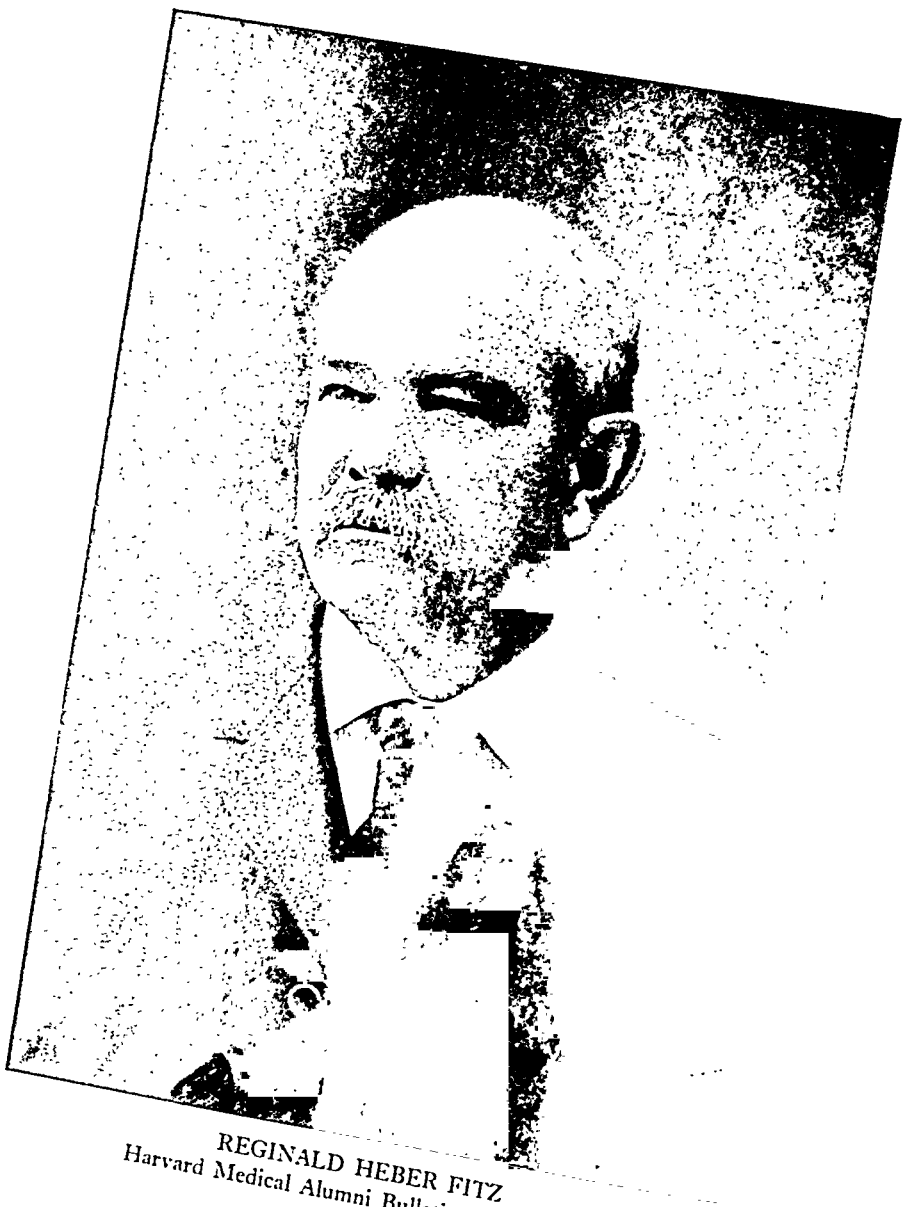
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Reginald Heber Fitz

BIOGRAPHY

- 1843 Born at Chelsea, Massachusetts. His father died young, leaving a widow with six children to support. Educated at the Chauncey Hall School.
- 1864 Age 21. Graduated from Harvard College.
- 1867 Age 24. Received an appointment as house officer at the Boston City Hospital.
- 1868 Age 25. Obtained the M.D. degree at Harvard and then traveled in Europe, studied in Vienna with Rokitansky and Skoda and in Berlin with Virchow.
- 1870 Age 27. Returned to Boston and became an instructor in microscopic pathology at the Harvard Medical School.
- 1873 Age 30. *Became an assistant professor.*
- 1878 Age 35. Became professor of pathological anatomy at Harvard and had charge of the pathological laboratory at the Massachusetts General Hospital.
- 1886 Age 43. Suggested the name appendicitis and made a classic report on this disease.
- 1887 Age 44. Became a visiting physician at the Massachusetts General Hospital.
- 1892 Age 49. Became professor of medicine at Harvard, occupying the Herseian Chair of the Theory and Practice of Physic.
- 1905 Age 62. Degree of LL.D. conferred on him by Harvard.
- 1909 Age 65. Retired from professorship at Harvard Medical School.
- 1913 Age 70. Died.

Member of the Massachusetts Medical Society.

Member of the Boston Society for Medical Observation.

Member of the Boston Society for Medical Improvement.

Member of the Boston Society of Medical Sciences.

President of the Boylston Medical Society of Harvard University.

Member and President in 1894 of the Association of American Physicians.

Member of the Interurban Club.

Member of the American Medical Association.

Member of the American Academy of Arts and Sciences.

BIBLIOGRAPHY OF WRITINGS

1. Belladonna versus opium. (Graduation thesis) Boston M. & S. J., 79: 272-282; 289-297, 1868.
2. Multilocular encysted disease of the cellular tissue, recurrent after operation. With H. J. Bigelow. Ibid., 84: 241-242, 1871.
3. Translation of "Ueber Lazarette und Baracken" by R. Virchow. Ibid., 84: 260-262, 1871.
4. A case of double monstrosity—union upon the anterior median line from clavicle to umbilicus. With H. O. Marcy. Ibid., 85: 17-20, 1871.
5. The theory of tuberculosis. A brief account of some of its more important features. Mass. Med. Soc., 3: 173-200, 1871.
6. Examination and drawings of spindle-celled sarcoma of choroid removed by operation. Boston M. & S. J., 86: 85-88, 1872.
7. Report on pathology and pathological anatomy. Ibid., 88: 393-397; 416-418, 1873; 89: 379-383; 401-405, 1874; 90: 381-383; 400-403, 1874; 91: 375-377; 401-404, 1875; 92: 438-443; 464-470, 1875; 93: 469-473; 496-503, 1875; 94: 446-450; 477-481, 1876; 95: 464-467; 492-496, 1876; 96: 405-410; 434-440, 1877; 97: 555-559; 587-591, 1877; 98: 666-670; 695-698, 1878; 99: 653-656; 692-696, 1878; 100: 710-715; 744-748, 1879; 101: 729-734; 766-770, 1879.

8. Translation, with A. Van Hurlington & J. T. Whittaker, of H. Sebert's Relapsing fever, typhus fever and cholera. *Cyclop. Pract. Med.* (Ziemssen), 1, 1874.
9. Tubo-uterine and interstitial pregnancy. *Am. J. M. Sc.*, n.s. 69: 95-103, 1875.
10. Anatomy of the fasciola Jacksoni. *New York M. J.*, 24: 513-518, 1876.
11. Rupture of the healthy esophagus. *Am. J. M. Sc.*, n.s. 73: 17-36, 1877.
12. Sudden death from embolism. *Boston M. & S. J.*, 96: 93-105, 1877.
13. The value of anatomical appearances. *Tr. Massachusetts Med.-Leg. Soc.*, 1: 14-24, 1878. Also: *Boston M. & S. J.*, 99: 168-178, 1878.
14. Fatal case of hydrophobia. *Ibid.*, 201-268, 1878.
15. Revised F. C. Shattuck & G. K. Sabine's translation of S. Orth's, A compend of diagnosis in pathological anatomy. 440 pp., 8°, Boston, Houghton, Osgood, 1878; 1879; 1880; 1882.
16. Diabetic coma; its relation to acetonaemia and fat embolism. *Boston M. & S. J.*, 104: 124-127; 132, 1881.
17. A case of hydrophobia of doubtful origin. By S. L. Abbot and R. H. Fitz. *Ibid.*, 147-150.
18. Diseases of the liver. Jaundice; cholecystotomy; hypertrophic cirrhoses. *Cyclop. Pract. Med.* (Ziemssen), N. Y., suppl., 467-473, 1881.
19. Persistent omphalo-mesenteric remains; their importance in the causation of intestinal duplication, cyst-formation and obstruction. *Am. J. M. Sc.*, n.s. 88: 30-57, 1884.
20. The recent investigations concerning the etiology of cholera. *Boston M. & S. J.*, 112: 169-172; 196-199, 1885.
21. Localized amyloid degeneration; amyloid lymphoma? *Ibid.*, 114: 389-390, 1886.
22. Perforating inflammation of the vermiform appendix, with special reference to its early diagnosis and treatment. *Tr. Assn. Am. Physicians, Phila.*, 1: 107-144, 1886. Also: *Am. J. M. Sc.*, n.s. 92: 321-346, 1886. Also, abstr.:

- Boston M. & S. J., 115: 113 only, 1886. Also, abstr.:
Ibid., 169: 626-627, 1913.
23. The origin of typhoid fever in hospitals, and the means suggested for its prevention. Boston M. & S. J., 118: 513-516, 1888.
 24. The relation of perforating inflammation of the vermiform appendix to perityphlitic abscess. New York M. J., 47: 505-508, 1888.
 25. The diagnosis and medical treatment of acute intestinal obstruction. Boston M. & S. J., 119: 445-449; 469-472; 493-495; 523-528, 1888. Also: Tr. Cong. Am. Phys. & Surg., 1888, 1: 1-42, 1889. Also: 64 pp., 12°, Boston, Cupples & Hurd, 1889.
 26. Acute pancreatitis: a consideration of pancreatic hemorrhage, hemorrhagic, suppurative, and gangrenous pancreatitis, and of disseminated fat-necrosis. Boston M. & S. J., 120: 181-187; 205-207; 229-235, 1889. Also: Med. Rec., N. Y., 35: 197-205; 225; 253, 1889. Also: Med. News, 54: 197; 225; 256; 281; 309, 1889. Also: Proc. New York Path. Soc. (1889), pp. 3-70, 1890.
 27. Letter. Typhloenteritis and appendicitis. Boston M. & S. J., 122: 167 only, 1890.
 28. Acute pancreatitis. Report of a case and reference to recent contributions. Ibid., 122: 572-575, 1890. Also: Tr. Assn. Am. Physicians, 5: 191-200, 1890.
 29. Appendicitis; some of the results of the analysis of seventy-two cases seen in the past four years. Boston M. & S. J., 122: 619-620, 1890.
 30. Henry Jacob Bigelow; a tribute of respect inspired by affection, admiration and obligation. Ibid., 123: 511-514, 1890.
 31. Perforating gastric ulcer; circumscribed peritonitis; death on the fifteenth day. Ibid., 123: 583 only, 1890.
 32. Intestinal perforation in typhoid fever; its prognosis and treatment. Tr. Assn. Am. Physicians, 6: 200-215, 1891. Also: Boston M. & S. J., 125: 346-348; 365-367, 1891.
 33. A case of amoebic dysentery. By E. P. Gerry and R. H. Fitz. Ibid., 125: 592, 1891.

34. The diagnosis and treatment of inflammation of the appendix. A discussion, at the Annual Meeting of the Massachusetts Medical Society, June 9, 1891. *Med. Communications Mass. Med. Soc.*, 15: 536-537, 1891.
35. The pathology of pelvic inflammation. *Boston M. & S. J.*, 126: 491-493, 1892. Also: *Am. Gynec. & Pediat.*, 5: 537-540, 1892.
36. The four years' course at the Harvard Medical School. *Boston M. & S. J.*, 126: 599-600, 1892.
37. Shall there be a four years' course? *Ibid.*, 127: 225, 1892.
38. Acute pancreatitis. *Ibid.*, 127: 571-572, 1892. Also: *Tr. Rhode Island M. Soc.*, 4: 452, 1893.
39. Lectures on Pathology. From the shorthand notes of Charles F. Allen, M.D. 3rd ed., Boston, MacDuffee & Palmer, 1892. (1st two editions were made up of typed or mimeographed sheets.)
40. The duties and dangers of the doctor's life. *Boston M. & S. J.*, 128: 303, 1893.
41. Intra-peritoneal hemorrhage. *Tr. M. & Chir. Fac. Maryland, Balt.*, pp. 83-95, 1893. Also: *Maryland M. J.*, 29: 155-163, 1893. Also: *Boston M. & S. J.*, 128: 618-621, 1893.
42. The rise and fall of the licensed physician in Massachusetts, 1781-1860. *Tr. Assn. Am. Physicians*, 9: 1-18, 1894. Also: *J. A. M. A.*, 22: 877-883, 1894. Also: *Boston M. & S. J.*, 130: 529-534, 1894.
43. The legislative control of medical practice. *Med. Communications Mass. Med. Soc.*, 16: 277-360, 1894. Also: *Boston M. & S. J.*, 130: 581-585; 609-613; 637-641; 131: 1-5; 25-27, 1894.
44. Diseases of the esophagus. In: *Twentieth Cent. Pract.*, 8°, N. Y., 8: 83-113, 1896.
45. The practice of medicine. By Horatio C. Wood and R. H. Fitz. 8°, Philadelphia, London, 1897.
46. Pneumonia; broncho-pneumonia; chronic fibrous pneumonia. *Syst. Pract. M. (Loomis)*, 2: 197-225, 1897.
47. Diabetes mellitus; with especial reference to its pancreatic

origin and to certain features of clinical interest and importance. *Yale M. J.*, 4: 275-291, 1897-8.

48. The significance of albumosuria in medical practice; suggested by a fatal case of albumosuric myxedema treated with thyroid extract. *Am. J. M. Sc.*, n.s. 116: 30-42, 1898. Also: *Tr. Assn. Am. Physicians*, 13: 8-22, 1898.
49. Diabetes mellitus at the Massachusetts General Hospital from 1874 to 1898. A study of the medical records. With E. P. Joslin. *J. A. M. A.*, 31: 165-171, 1898. Also: *Am. Med.-Surg. Bull.*, 12: 861-868, 1898.
50. Aneurism of the arch of the aorta with radiograph. (Brief case report). *Boston M. & S. J.*, 139: 413, 1898.
51. Successful resection of the pylorus for cancer. (Brief case report). *Ibid.*, 139: 413, 1898.
52. The relation of idiopathic dilatation of the colon to phantom tumor, and the appropriate treatment of suitable cases of these affections by resection of the sigmoid flexure. *Am. J. M. Sc.*, 118: 125-137, 1899.
53. Multilocular cystoma of the pancreas. *Tr. Assn. Am. Physicians*, 15: 254-261, 1900. Also: *Am. J. M. Sc.*, 120: 184-190, 1900.
54. Some surgical tendencies from a medical point of view. *Med. News*, 79: 1009-1015, 1901. Also: *Boston M. & S. J.*, 145: 693-699, 1901.
55. Certain characteristics of osteitis deformans. *Am. J. M. Sc.*, n.s. 124: 814-825, 1902. Also: *Tr. Assn. Am. Physicians*, 17: 398-405, 1902.
56. Typhoid fever at the Massachusetts General Hospital during the past seventy-eight years. Mortality; intestinal hemorrhage; perforation; relapse. 14 pp., 8°, 1902.
57. Additions to Diseases of the liver, pancreas and suprarenal capsules, by L. Oser, E. Neusser, H. Quincke, G. Hoppe-Seyler, etc., Phila., Saunders, 1903.
58. Herpetiform and bullous dermatitis. (Case) *Boston M. & S. J.*, 148: 343-344, 1903.
59. Chonro-dystrophic dwarf. (Case) *Ibid.*, 148: 344-346, 1903.

- o. The clinical significance of arteriosclerosis. *Ibid.*, 148: 357-359, 1903.
1. The pancreas and pancreatic diseases. The symptomatology and diagnosis of diseases of the pancreas. *Trans. Cong. Am. Phys. & Surg.*, 6: 36-54, 1903. Also: *Boston M. & S. J.*, 148: 601-608, 1903. Also: *Am. Med.*, Phila., 5: 907-912, 1903.
2. Some observations on appendicitis. *Boston M. & S. J.*, 151: 339-341, 1905.
3. A brief consideration of some of the results of the surgical treatment of cancer of the stomach. *Ibid.*, 152: 65-66, 1905.
4. Intrapleural lipoma; acute pericarditis; pericardial exploration. *Am. J. M. Sc.*, n.s. 130: 785-789, 1905.
5. The borderland of medicine and surgery. *Boston M. & S. J.*, 156: 655-662, 1907.
6. The early diagnosis of gall stones. *Yale M. J.*, 15: 209-222, 1908-9.
7. Zabdiel Boylston, inoculator and the epidemic of smallpox in Boston in 1721. *Johns Hopkins Hosp. Bull.*, 22: 315-327, 1911.
8. The diagnosis of abdominal disease. An address before the Springfield Academy of Medicine, Springfield, Mass., Nov. 14, 1911. Printed by request.
9. The introduction of inoculation. (Letter) *Boston M. & S. J.*, 166: 356-357, 1912.
- o. Continuous versus interrupted hospital service. *Ibid.*, 166: 399-400, 1912.
1. Memorial to Maurice Howe Richardson, M.D. *Ibid.*, 167: 903-907, 1912.

BIBLIOGRAPHY OF BIOGRAPHIES

- To R. H. Fitz, in honor of his 65th birthday, May 5, 1908. *Boston M. & S. J.*, 158: 605-748, 1908.
- Biography by A. K. Stone. *Bull. Harvard M. Alumni Assn.*, n.s. 6: 71-75, 1908. Also: *Pub. Mass. Gen. Hosp.*, 2: 350-354, 1908.

- Memorial addresses by W. W. Keen and C. W. Eliot. Meeting Held at the Harvard Medical School, Boston, Mass., Nov. 17, 1913. Jamaica Plain, Jamaica Pr. Co., 45 pp., 8°, 1913.
- Biography by F. C. Shattuck. Harvard Grad. Mag., 22, 1913.
- Dr. Fitz's services to surgery. By W. W. Keen. Boston M. & S. J., 169: 893-895, 1913.
- Dr. Fitz's contribution to pathology. By W. T. Councilman. Ibid., 169: 895-897, 1913.
- Dr. Fitz as a teacher. By W. S. Thayer. Ibid., 169: 897-898, 1913.
- Dr. Fitz's association with the Massachusetts General Hospital. By H. P. Walcott. Ibid., 169: 899-901, 1913.
- Dr. Fitz's service to medical education. By C. W. Eliot. Ibid., 169: 901-903, 1913.
- Obituary. J. A. M. A., 161: 1390, 1913.
- Obituary. Med. Rec., N. Y., 84: 626, 1913.
- Obituary. Johns Hopkins Hosp. Bull., 25: 87-89, 1914.
- Biography by H. A. Kelly. Boston M. & S. J., 180: 75-78, 1919.
- Biography. Medical Life, 29: 323, 1922.
- Biography. Med. Rev. of Rev., 34, 1928.
- Biographical sketch and abstract of article of 1886 on appendicitis. In: Classic Descriptions of Disease by R. H. Major. Springfield, Ill., Thomas, 1932, pp. 620-622.
- Biographic note by Reginald Fitz. Harvard Med. Alumni Bull., 7: 42-45, 1933.

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TRANSACTIONS

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Perforating Inflammation of the Vermiform Appendix; with Special Reference to its Early Diagnosis and Treatment

BY

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IT APPEARS that even the most recent systematic writers are by no means agreed as to the exact relation of inflammation of the cecum and that of the appendix to peritonitis and perityphilitis. The vital importance of the timely and appropriate treatment of the disease in question is becoming more and more apparent. Such treatment is often postponed till hopeless, even if its application is at any time entertained. It was, therefore, to be anticipated that the critical consideration of a large number of unquestionable cases of perforation of the cecal appendix might serve to make prominent the features essential for diagnosis and treatment.

In 1834, James Copland, in his *Dictionary of Practical Medicine*,¹ first discriminated between inflammations of the caecum, the vermiform appendix, and the pericaecal tissue. Isolated cases of fatal inflammation of the appendix had been published from time to time before this date. Their importance did not

¹ Vol. i. p. 277.

become well recognized, however, till after Dupuytren's views had been made known concerning the relation of the caecum to the production of what had hitherto been termed iliac abscess, or phlegmon of the iliac fossa. At the instigation of this eminent surgeon, Husson and Dance¹ published an article on the subject, apparently expressing his ideas. These were subsequently personally presented by him in his *Lectures on Clinical Surgery*.²

In consequence of the interest thus aroused, Goldbeck,³ at the suggestion (p. 108) of Puchelt, of Heidelberg, wrote his graduation-thesis upon the same subject. He adopted the views of the French writers, and applied the term perityphilitis to the disease described. His essay contains the report of a case of perforation of the appendix and associated peritonitis. But he regards it as one of fecal retention, and as quite distinct from the perityphilitis or inflammation of the connective tissue around the caecum. He states that in fatal cases of the latter affection the appendix has been found intact.

Of the various names connected with the early history of the disease under consideration that of John Burne, Physician to the Westminster Hospital, deserves particular mention. In the first⁴ of two admirable articles separated by an interval of two years, he calls attention to the material difference in the character of inflammation of the appendix and that of the caecum. He attributes this difference to the peculiar conformation and situation of the former. His second paper⁵ contains an additional number of cases of affections of the caecum and appendix, a criticism of the opinions of the French writers, and a reiteration of his own views with such modifications as a more extended experience permitted. The name typhlo-enteritis is offered as an equivalent for inflammation and perforative ulceration of the caecum and of the appendix.

In the interval between the publication of the above-mentioned articles, Albers⁶ contributed a paper on inflammation of the

¹ Répertoire Gén. d'Anat., etc., 4: 154, 1827.

² Leçons Orales de Clin. Chir., 3: 330, 1833.

³ Ueber eigenth. entz. Geschw. i. d. rechten Hüftbeingegegend, 1830.

⁴ Med.-Chir. Trans., 20: 219, 1837.

⁵ Ibid., 22: 33, 1839.

⁶ Beob. auf d. Geb. d. Path. und Path. Anat., 1, 1838.

caecum. He first introduces the term typhilitis and perityphlitis. He charges Puchelt and foreign writers with confounding the last affection with the acute and stercoral varieties of typhilitis. The frequent termination of the perityphlitis in abscess is recognized, likewise the possibility of communication between the pus-cavity and that of the appendix or caecum. This communication he regards as secondary. He says,¹ "It is not at all clear just why the *processus vermiformis* should be so often affected, for in this disease perforation of the caecum should be far more likely than that of the appendix."

Although the term perityphlitis thus became synonymous with inflammation of the pericaecal tissue, the tendency was inevitably (p. 109) toward the recognition of a somewhat similar clinical picture and a different anatomical seat. Oppolzer² discriminated between cases of perityphlitis where the inflammation was situated in the connective tissue about the caecum, and others where the inflammatory swelling lay between the iliac fascia and the bone. These were further distinguished from cases of encysted peritonitis in this region, and from perforation of the appendix. The latter was stated to be always productive of a circumscribed peritonitis, except when the perforation took place through the adherent peritoneum. Then both peritonitis and inflammation of the subperitoneal tissue would occur. The anatomical seat of the inflammatory process was thus further complicated. Oppolzer suggested the term paratyphlitis, which, according to Eichhorst,³ represents an inflammation of the connective tissue behind the caecum, while perityphlitis designates an inflammation of the peritoneal coat of the caecum and appendix. Typhlitis is applied to an inflammation of the appendix and of the caecum. Whittaker⁴ uses the same definitions, while Ziegler⁵ applies the term typhlitis to inflammation of the vermiform appendix, and perityphlitis to that of the parts in its vicinity.

¹ Op. cit., p. 19.

² Allg. Wiener med. Zeitung, 20: 81; 21: 86, 1858.

³ Handb. d. Spec. Path. und Therap., 2: 188, 1885.

⁴ Pepper's System of Pract. Med., 2: 814, 1885.

⁵ Lehrb. d. Path. Anat., 4te Aufl., 2: 1, 1885.

The clinician obviously recognizes as of the chiefest importance the parts to which local treatment may be directly applied. His attention is thus conspicuously directed to the caecum, which may be evacuated, or to the perityphlitic abscess, which may be emptied. The pathologist looks for the seat and causes of the disease, and finds that in most fatal cases of typhlitis the caecum is intact, while the appendix is ulcerated and perforated. He sees that the so-called perityphlitic abscess exists in the pericaecal fibrous tissue; it is in most instances caused by an inflamed appendix. Finally, if the encysted peritoneal abscess, or the abscess in fibrous tissue behind the caecum, does communicate with the latter, such an opening is usually the result, not the cause, of this abscess.

With,¹ influenced by the predominant importance of the independent consideration of inflammation of the appendix and its results, uses the term appendicular peritonitis to indicate the perityphlitis proceeding (p. 110) from disease of the appendix. As a circumscribed peritonitis is simple one event, although usually the most important, in the history of inflammation of the appendix, it seems preferable to use the term appendicitis to express the primary condition. This may terminate as an appendicular peritonitis or as a paratyphlitis. In like manner the rare, primary, perforating typhlitis (caecal perforation) may be followed by a perityphlitis—that is, an encysted peritonitis about the caecum, or by a paratyphlitis. The perityphlitic abscess of the surgeon, when seen early, is thus usually an encysted peritonitis of appendicular origin. More rarely, at this date, it may be the result of a suppurative paratyphlitis. The causes of this last affection are numerous and by no means confined to the appendix or caecum, although a perforating inflammation of each of these parts of the intestinal tract may act as a cause.

Any attempt at explaining the various results of an inflammation of the appendix must necessarily be preceded by a statement of the peculiarities it may present with respect to structure and position. These peculiarities, though in part of congenital origin, in most instances bear evidence of having been acquired

¹ Nordiskt Med. Ark., vii. 1. London Med. Record, 8: 213, 1880.

as the result of previous disease. This statement, based upon a long personal experience, is more than confirmed by the observations made elsewhere. Matterstock¹ states that Tüngel, during a period of two years at the Hamburg Hospital, found 30 instances of partial or complete obliteration of the appendix, 43 cases of catarrh and fecal concretions, 12 of abnormal adhesions, and 11 of tuberculous ulcers. All these in addition to perforations, and despite the fact that attention was not invariably directed to such peculiarities. Toft, as referred to by With,² found the appendix diseased in 110 out of 300 post-mortem examinations, every third person thus possessing a diseased appendix.

Personal observations have enabled me to recognize considerable variations in the length of the appendix, the longest being nearly six inches. Wister³ alludes to one which was nine inches long. It is frequently seen with an attached fold of peritoneum and fat tissue, suggesting an omentum or mesentery. Its free end has been found in the iliac fossa, as well as behind the caecum; along the brim of the pelvis and hanging into the cavity of the latter. Irregular positions (p. 111) have often been associated with fibrous adhesions. The appendix has been found thus attached not only in the places above mentioned, but also with its tip directed upward and its course more or less parallel with that of the caecum, either behind, to the right, or to the left of this structure. It has also been found adherent to the mesentery with its tip bent at right angles and lying between the appendix and this structure. Kraussold⁴ observed its course directed upward and backward, forming a loop around the ileum with its tip directed forward. It has been seen pointing outward, then forward, forming a loop around the lower end of the caecum with its tip behind the latter.

Firket⁵ records the adherence of the appendix to the ileum throughout the length of the former, with a communication

¹ Gerhardt's Handb. d. Kinderkrankh., 4: 897, 1850

² Loc. cit.

³ Trans. Coll. Phys. Philada., n.s. 3: 147, 1856-62.

⁴ Volkmann's Samml. klin. Vortr., 191: 1757, 1881.

⁵ Ann. d. l. Soc. Méd.-Chir. d. Liège, 21: 58, 1882.

between the cavities of the two and without an evident ulceration of the mucous membrane. Adherence to the rectum with a communication between the cavities of each is recorded.¹ Adhesions of the tip to the mesentery, the rectum, and bladder are frequent. Its presence in a hernial canal led Shaw² to suspect a disease of the testicle. Thurmman³ records a like occurrence, and the formation of a scrotal tumor as large as the two fists in consequence of an inflammation of the appendix. Its tip has been found⁴ adherent to the abdominal wall in the vicinity of the navel, and pus has been discharged from it at this point.

Complete or partial obliterations of the canal are frequent. In the former instance a solid cord results. In the latter, a considerable cystic dilation of the tip may follow; or a funnel-shaped pouch at the origin is often associated with obliteration of the remaining portion of the tube.

These variations in length, position, and patency, whether congenital or acquired, are of obvious importance in explaining many of the apparent differences in the clinical histories of typhlitis and perityphlitis. Their significance in the etiology of appendicitis will appear directly.

The presence of foreign bodies in the canal of the appendix is of frequent occurrence. These are a variety of seeds, especially of fruit. Less common are hairs, particularly bristles, worms of their eggs, shot, pins, lipsls, and gall-stones. By far the most numerous are (p. 112) moulded masses of inspissated feces, more or less cylindrical in shape and of extreme variation in density. Some are of the consistency of normal excrement, while others are of stony hardness in consequence of their infiltration with earthy salts. The relative frequency of their presence in the appendix is manifested by the records of fatal cases of appendicitis, but their actual frequency far exceeds the number of these cases. In my own experience, it is rather the rule than the exception for the appendix to contain moulded, more or less inspissated feces.

¹ Trans. Lond. Path. Soc., 27: 161, 1876.

² Ibid., 1: 270, 1848.

³ Prov. Med. and Surg. Journ., 477, 1848.

⁴ Lancet, 2: 565, 1839-40.

The frequency of such retention may be due to the congenital or acquired peculiarities of the appendix already described. German writers attach a certain importance to the presence of a valve-like projection of mucous membrane, discovered by Gerlach,¹ at the mouth of the appendix. Although a pinhole opening may result, any considerable obstruction must be of extreme rarity. The habits of individuals with reference to diet and regulation of the bowels are of unquestioned importance. Equally significant is the controlling fact that most persons suffering from habitual constipation and accustomed to swallow the seeds of fruit, escape inflammation of the appendix.

Recognizing the lack of agreement in the use of the term typhlitis and perityphlitis, a collection has been made of 257 cases of perforating inflammation of the appendix. By limiting the attention to the essential features of these cases, it was thought possible to recognize the characteristics of this sharply defined affection, by means of which it might be differentiated from all others occurring in this region. At the same time a comparison is drawn between many of these characteristics and those occurring in cases of typhlitis and perityphlitis. The latter terms are sufficiently indicative of a clinical picture, although its seats and causes suggest the importance of shades of distinction; 209 of these cases have been collected, and serve as the basis of a series of tables to be contrasted with those obtained from the analysis of the 257 cases of appendicitis.

The etiological importance of the presence of fecal masses and of foreign bodies in the production of inflammation of the appendix is well recognized. Matterstock² found in 169 cases of fatal perforating appendicitis, that fecal concretions were present in 53 per cent, and foreign bodies in 12 per cent. In the series here collected, out of 152 (p. 113) cases the percentage³ of fecal masses was 47 per cent, that of foreign bodies 12 per cent. It thus appears that in nearly one-half of the cases more or less inspissated feces were found, and that in nearly one-eighth of the series foreign bodies other than feces were present. Thus,

¹ Zeitschr. f. rat med., 6: 12, 1847.

² Op. cit.

³ In general whenever percentages are given, fractions will be disregarded.

in about three-fifths of all cases of perforating inflammation of the appendix either dried feces or foreign bodies were present in the tube. When seeds are stated to have been found, the evidence is not always sufficient to exclude the possibility of a mistake having been made as to the nature of the foreign body. Notwithstanding this large percentage, the reality is undoubtedly much greater. Many are overlooked at the time of making the examination, others are macerated in the contents of the abscess. Still others, perhaps, escape with the pus, which makes its way outward through the various channels by which the abscess may communicate with the surface of the body.

The frequent immunity of the appendix from inflammation in the presence of inspissated feces and foreign bodies suggests the importance of other factors in the etiology. External violence is occasionally recorded as an immediate precursor of the attack. Among the 257 cases were 19 who were supposed to have received an injury, the result rather of indirect than of direct violence; from lifting a heavy weight in 9 instances, and from a fall or blow in 10. Among 209 cases of typhlitis and perityphlitis external violence immediately preceded the attack of the disease in 10 per cent.

Disgestive disturbances are of obvious importance in the etiology of inflammation of the appendix, since this organ is a part of the alimentary canal. There were 15 instances of prolonged constipation, 9 of diarrhoea, and 6 of vomiting. The attacks of diarrhoea and vomiting were usually the result of indiscretion in diet, but they were sometimes occasioned by the use of domestic remedies. These were administered for the relief of constipation or other disturbances attributed to a sluggish action of the stomach and bowels.

Among the cases of typhlitis and perityphlitis were 38 of constipation, 15 of diarrhoea, and 3 of vomiting; these symptoms being of apparent etiological importance.

Notwithstanding the frequency of typhoid fever and of intestinal tuberculosis, in which affections the mucous membrane of the appendix is often diseased, a resulting perforation seems to have been relatively (p. 114) infrequent. There were 8 of

a perforating ulcer of the tuberculous appendix, and 3 of this lesion in convalescence from typhoid fever.

Among the 209 cases of typhlitis and perityphlitis were 2 occurring in tuberculous persons.

The consideration of sex in 247 cases gives the following results: 197 males, 80 per cent, and 50 females, 20 per cent. These percentages are the same as those found by Fenwick¹ in the analysis of 130 cases.

In 209 cases of typhlitis and perityphlitis there were 156 males, and 53 females; 74 per cent of the former, and 26 per cent of the latter.

The age in 228 cases of appendicitis is recorded as follows:

From 20 months to 10 years.....	22 = 10 per cent.
" 10 years " 20 "	86 = 38 " "
" 20 " " 30 "	65 = 28 " "
" 30 " " 40 "	34 = 15 " "
" 40 " " 50 "	8 = 3 " "
" 50 " " 60 "	11 = 5 " "
" 60 " " 70 "	1 = $\frac{1}{2}$ " "
" 70 " " 78 "	1 = $\frac{1}{2}$ " "

The age of the youngest patient was 20 months, that of the oldest, 78 years; 173 cases, 76 per cent of the entire list, were under the age of 40 years, and nearly 50 per cent were under the age of 20 years. Fenwick's² table of ages is based upon the consideration of 97 cases, and shows smaller percentages for the several decades up to the age of 40 years.

The age of the patient in 178 cases of typhlitis and perityphlitis was:

From 4 years to 10 years.....	10 = 6 per cent.
" 10 " " 20 "	53 = 30 " "
" 20 " " 30 "	53 = 30 " "
" 30 " " 40 "	25 = 14 " "
" 40 " " 50 "	18 = 10 " "
" 50 " " 60 "	10 = 6 " "
" 60 " " 70 "	7 = 4 " "
" 70 " " 78 "	2 = 1 " "

¹ Lancet, 2: 987; 1039, 1884.

² Loc. cit.

From the above consideration it is apparent that perforating appendicitis is a disease most frequently occurring among healthy youths (p. 115) and young adults, especially males. Further, that attacks of indigestion and acts of violence, particularly from lifting, jumping, and falling, are exciting causes in one-fifth of the cases. A local cause is to be found in more than three-fifths of all cases in the retention in the appendix of more or less inspissated feces, or in the presence there of a foreign body. The retention of feces may be promoted by a constipated habit, but congenital or acquired irregularities in the position and attachments of the appendix frequently act as favoring causes. A fact in support of the last-mentioned statement is to be found in the frequency of successive attacks, one or more, of inflammation of the appendix. Among 257 cases were 28, 11 per cent, which presented similar symptoms of greater or less severity, at various intervals before the final attack. Recurrence is mentioned in 23 out of 209 cases, again 11 per cent, of typhlitis and perityphlitis.

The inflammatory process once excited, its course and results show extreme variations. A simple catarrhal appendicitis is to be recognized anatomically, but it is doubtful whether its clinical appreciation is possible. This appendicitis, in the absence of a concretion or foreign body, may progress toward ulceration, even to a peritonitis, which may terminate fatally. In the presence of a foreign body or concretion these events are of likely occurrence. On the one hand, the inflammation may result in the more or less complete obliteration of the canal of the appendix, with or without circumscribed dilatation. On the other, the ulcerative process becomes associated with a necrosis of the wall, a peritonitis, usually circumscribed at the onset, and perforation. In those cases where the appendicular peritonitis represents the extension of an inflammation through the wall of the appendix without perforation, permanent adhesions of the appendix to neighboring parts remain as evidence of the process. When it is associated with necrosis of the wall, the inflammation of the peritoneal coat tends to become diffused and productive of serous and cellular exudations. The adherence

of coils of intestine to each other and to the abdominal wall favors the accumulation of the exudation in a limited space, and thus the formation of the tumor. At this stage the anatomical condition is a circumscribed peritonitis, the appendicular peritonitis of With. In certain instances the term perityphlitis might be applied in an exact anatomical sense, as the peritoneal inflammation frequently extends to the serous investment of (p. 116) the lower part of the caecum. But in the last two cases of fatal appendicitis examined by me, the appendicular peritonitis was wholly pelvic. The changes observed in the appearance of the serous covering of the caecum were of the same character as those affecting the peritoneum elsewhere. This peritoneal abscess may then become absorbed, or its contents may escape into the general peritoneal cavity through ruptured or softened adhesions. In the latter event, as a rule, death rapidly follows. The exceptional case reported by Markoe¹ may be regarded as one of extreme rarity. A child with symptoms of general peritonitis on the second day, died a month later from another disease. The appendix had been perforated and the intestines were adherent in different places.

The product of the circumscribed peritonitis varies exceedingly in quality and quantity. Although it is usually thin, discolored, and very offensive, it may be thick, yellow and odorless. In the postmortem examination of a case of recent occurrence, where general peritonitis was the cause of death, the abscess contained perhaps an ounce of pus. The peritonitis was the result of a secondary mesenteric thrombophlebitis, where the primary appendicular peritonitis was apparently in a retrograde condition. The acute stage of the disease lasted more than six weeks. Barrett² states that he removed from a perityphlitic abscess, on the sixty-second day, more than a gallon of pus, liquid feces, and scybala. The presence of the last element indicates a communication with the large intestine.

If the case does not terminate as thus stated, the tumor may suddenly diminish in size with the discharge of pus from a

¹ Am. Med. Monthly, 8: 231, 1857.

² Va. Med. Monthly, 2: 120, 1875-76.

hollow organ, as the intestine, bladder, or vagina. The anterior abdominal wall may become perforated and a sinus be established opening in the groin, lumbar region, or at the umbilicus. Shaw¹ mentions the occurrence of multiple abscesses of the scrotum from a perforated hernial appendix, and Thurmann² records a similar instance. Such sinuses often remain open for a long time, even many years. Through the kindness of Dr. A. T. Cabot, of Boston, I saw a patient with a fecal fistula which had existed for nineteen months. At the outset a tender swelling in the right groin had been incised, but the wound never (p. 117) healed. After an operation to promote the healing of the sinus, about an inch of the perforated appendix protruded from the wound. A similar protrusion had taken place six months earlier. The outer surface of the appendix was smooth, of a dusky red color, and the margin of the opening was sharply defined. Pressure upon the abdominal wall over the caecum, caused soft, yellow, intestinal contents to appear in the wound.

The abscess may contain sloughs of tissue and yet be intraperitoneal. In a recent post-mortem examination I removed from the encysted abscess around the appendix, a slough, three inches in length representing the detached peripheral portion of the tube. Ballou³ records a case where the sloughed appendix was discharged per anum, the patient recovering. In the case reported by Pooley,⁴ apparently the entire appendix escaped as a slough from the wound.

The more protracted the course of the disease the greater is the probability of the destruction of the peritoneum forming the wall of the abscess. With the perforation of the parietal peritoneum may occur extensive necrosis, purulent and fecal infiltration of the abdominal walls. Within three weeks the iliac muscle may be destroyed and the ilium be bared. The course of the psoas and iliacus may be followed into the thigh, and extensive and deep-seated destruction of tissue with fecal

¹ Loc. cit.

² Loc. cit.

³ Trans. R. I. Med. Soc., 2: 418, 1877-82.

⁴ N. Y. Med. Record, 10: 267, 1875.

infiltration be present in this region. The pus may extend through the obturator foramen, forming a deep-seated abscess of the hip and thigh, and may enter the hip-joint.

Moore¹ has shown that disease of the hip-joint may follow perityphlitis, and Gibney² has called attention to the possibility of mistaking cases of perityphlitis for disease of the hip-joint. The primary appendicular peritonitis may in like manner be continued into the tissues behind the caecum, and thus a secondary paratyphlitis or perityphlitic abscess be occasioned. So various are these possibilities that every case of so-called perityphlitic abscess must be regarded as primarily one of a perforating appendicitis unless proven to be the contrary.

With the frequent eventual destruction of the peritoneal wall of the abscess is the possibility of death from hemorrhage. Conant³ describes the case of a young man who died at the end of three weeks. There (p. 118) was no general peritonitis, but the abscess communicated with the caecum (the appendix being destroyed) and held a pint of clotted blood. Fatal hemorrhage from ulceration of the deep circumflex iliac artery is recorded by Bryant.⁴ This case is not unlikely to have been one of appendicitis, although the condition of the appendix is not stated. Again, Powell⁵ reports a case where the appendix was adherent to the internal iliac artery, the cavities of the two being in communication. The colon and caecum were distended with gas and dark blood.

The occurrence of disease of remote parts may be alluded to, as abscesses of the liver from pylephlebitis or portal embolism in consequence of a mesenteric thrombophlebitis near the appendix. The affection of the liver and portal vein may be the result of a direct continuance of the phlebitis, or may follow putrid embolism from a thrombus in the immediate vicinity of the appendix. The extension of a secondary paratyphlitis

¹ Lancet, 2: 514, 1864.

² Am. Journ. Med. Sci., 81, 1881.

³ Am. Med. Monthly, 1858, x. 359.

⁴ British Med. Journ., 2: 43, 1884.

⁵ N. O. Med. and Surg. Journ., 11: 468, 1855.

may cause perforation of the diaphragm with a consecutive pleurisy or pericarditis.

In considering the symptoms of appendicitis, it is to be noted that attacks of inflammation frequently occur without giving rise to any characteristic symptoms, and often without a suggestion of any distinct malady.

A comparison of the results of post-mortem examinations with the records of the previous histories of patients justifies this statement, unless it be urged that the disease occurred so early in life as to have been unappreciated or forgotten. Out of 227 cases of perforated appendix, however, 22, about 10 per cent, were under the age of ten years. This number is far too small to account for the occurrence of evidences of disease of the appendix in more than one out of every three autopsies.

The records of the Massachusetts General Hospital state that an individual with an appendix a half inch long, thickened, curved, and intimately adherent to the thickened and opaque subjacent peritoneum, never had symptoms of inflammation in this region. Another patient was never sick before his fatal illness, although the appendix and caecum were closely united to the neighboring parts by old fibrous adhesions, and the canal of the appendix was obliterated. Still another patient was always well and strong till within eleven days of (p. 119) his death, yet the appendix was converted into a solid fibrous band intimately united by firm adhesions to the posterior wall of the caecum. The severity of these lesions suggests the probability that apparently slight disturbances of digestion were overlooked. The diarrhoea, constipation, or abdominal pain, especially when occasionally recurrent, were regarded as characteristic of a feeble digestion. There can be little doubt that a diagnosis of bilious attack, colic, gastritis, enteritis, gravel, ovaritis, congestion of the womb and the like, may not infrequently conceal the existence of an inflamed appendix.

The latency of the symptoms in certain cases of appendicitis is such that the eventual diagnosis is obscured, and the desirable method of treatment hopelessly postponed. Buck¹ reports that a sailor was at work rolling barrels of flour till the day of his

¹ New York Medical Journal, 2: 40, 1866.

admission to the hospital. He then had a prominent iliac tumor extending along the outer half of Poupart's ligament. Fluctuation was transmitted from it to below the inner half of the ligament. Another sailor left Portland for New York, April 12, 1886, and arrived five days later. In the meantime he purged himself in consequence of a right iliac pain. Although suffering, he kept at work during the following week. He then left for Boston, where he arrived on the thirteenth day after the beginning of the pain. Symptoms of general peritonitis were evident, and he died the next day. General peritonitis was present, the result of an encysted inflammation about the appendix. This organ formed a gangrenous slough lying in the cavity of the abscess.

The latency, as well as the frequent obscurity, of the symptoms of appendicular inflammation is thus apparent. The presence, therefore, of the symptoms now to be mentioned, in individuals from whom the history of one, and particularly of several such attacks is to be obtained, is of marked importance in aiding diagnosis.

Sudden, severe abdominal pain is the most constant, first, decided symptom of perforating inflammation of the appendix. It occurred in 216 out of 257 cases, 84 per cent. In most instances it is present in apparently healthy individuals, in a few it follows an attack of diarrhoea.

The pain is usually intense, rarely slight, and is occasionally accompanied by a chill, or nausea and vomiting (p. 120). The following tables shows its localization in 213 cases of appendicitis, and, by way of contrast, in 92 cases of typhlitis and perityphlitis:

	Appendicitis Cases	Per Cent.	Typhlitis & Perityphlitis Cases	Per Cent.
In right iliac fossa.....	103	= 48	55	= 60
" abdomen.....	76	= 36	31	= 34
" hypogastrium.....	11	= 5	0	
" umbilical region.....	9	= 4	2	= 2
" epigastrium.....	4	= 2	4	= 4
" stomach.....	3	= 1	0	
" hepatic region.....	3	= 1	0	
" left iliac fossa.....	3	= 1	0	
" right hip and groin.....	1	= $\frac{1}{2}$	0	
Total.....	213		92	

It is quite probable that the number of cases of more exactly localized pain would have been considerably greater had attention been specially directed to this point. Many of the recorded cases of abdominal and hypogastric pain would undoubtedly have permitted a more definite localization, especially as firm pressure often discloses a sensitive spot at some distance from the referred seat. Though usually limited to the fossa, the pain sometimes extends upward as far as the liver, or downward to the rectum, testicle, perineum, or thigh. The attack is occasionally associated with great nervous anxiety, and is at times followed by marked prostration from which the patient rallies in the course of a few hours.

This sudden intense pain is presumably due, not to the actual beginning of the disease, but to the separation of the fresh adhesions of an acute appendicular peritonitis, and often, perhaps usually, to the perforation of the inflamed appendix. It generally represents the beginning of a more extensive peritonitis. An attempt has been made to ascertain the date of occurrence of this most important symptom. This was possible in 61 cases of appendicitis, and in 64 cases of typhlitis and perityphlitis. It occurred as follows:

	Appendicitis		Typhlitis & Perityphlitis	
	Cases	Per Cent.	Cases	Per Cent.
On the 1st day in.....	41	= 67	48	= 75
" " 2nd " ".....	5	= 8	10	= 16
" " 3rd " ".....	12	= 20	2	= 3
" " 4th " ".....	2	= 3	4	= 6
" " 5th " ".....	1	= 2	0	
Total.....	61		64	

(p. 121)

If the pain is not accompanied by nausea and vomiting, these symptoms are not unlikely to follow. Their occurrence is recorded in 15 cases of appendicitis, and in 44 out of 209 cases of typhlitis and perityphlitis. The vomit quickly becomes green in color, but in general this symptom is not distressing at this stage of the disease. Diarrhoea is rarely present, while constipation is the rule.

The abdominal pain is followed by fever as the next constant symptom. The date of its appearance is noted in but 38 cases of appendicitis, and in only 16 of typhlitis and perityphlitis. It was present

	Appendicitis	Typhlitis & Perityphlitis
On the first day in.....	5 cases	6 cases
" " 2nd " ".....	18 "	7 "
" " 3rd " ".....	9 "	0 "
" " 4th " ".....	6 "	3 "
	<hr/> 38 cases	<hr/> 16 cases

The temperature is rarely very high, and the constitutional disturbances usually associated with an elevated temperature are frequently slight, if not absent. The maximum recorded in the cases here collected is 103.5°F., but the range is usually between 100°F. and 102°F. With¹ noticed an elevation of nearly 106°F. If violent or extreme changes take place, a complication may be expected, as an abscess of the liver, or a pleurisy from an extension of the local inflammatory process.

During the first three days following the onset of the pain, micturition is occasionally disturbed. Perhaps unusually frequent on the first day, it is likely to be difficult on or after the third day. In certain instances the use of the catheter is required. A satisfactory explanation of this latter feature is to be found in the abundant use of opium usually necessary at this stage of the disease. The right testicle may be retracted and swollen, in which case the course of the pain is apt to be toward this gland.

The circumscribed swelling in the right iliac fossa now demands consideration. This symptom, when present, is evidently of the upmost value in diagnosis, as its appropriate treatment most favorably modifies the prognosis. The swelling represents the accumulation of (p. 122) the increasing exudation, at the outset the product of the peritonitis, and lies beneath the adherent coils of intestine which later become attached to the abdominal walls.

¹ Loc. cit.

Its usual seat is in the right iliac fossa, below a line extending from the anterior superior spine of the ilium to the navel, nearer the former and two finger-breadths above Poupart's ligament. It may lie nearer the median line or may approximate the iliac crest. The swelling may be found in the pelvis in those cases where the appendix becomes attached to the peritoneum of the pelvic wall. It is rare for the primary swelling to be paracaecal, although this variety occurs where the appendix lies embedded behind the caecum.

The early products of the peritonitis are largely cellular and fibrinous; scanty, opaque, greenish masses are found encapsulated. This condition is obviously not to be recognized by physical signs. As the liquid exudation increases, dulness becomes apparent. This sign may be obscured by intervening and adherent coils of intestine, especially if they are distended with gas, when a superficial gurgling may be recognized. Again, the contents of the abscess may be partly gaseous, a condition more likely to occur later in the course of the disease. A circumscribed resistance is felt on palpation. As the part is often extremely sensitive to pressure and the abdominal muscles tense, the administration of ether or chloroform may be necessary to confirm the diagnosis. A rectal examination not infrequently permits the recognition of the tumor which abdominal palpation fails to disclose, and should always be made in the latter event. Owing to the position of the abscess beneath the transversalis fascia, and to the fact that it is often covered by adherent coils of intestine, a sense of fluctuation is rarely perceived till much later in the history of the case.

The clinical characteristics of the tumor and its composition are thus made evident by modified resonance on percussion, circumscribed resistance on palpation, and a sense of fluctuation. Notwithstanding the importance of these signs, the records of 257 cases of appendicitis give comparatively little information with reference to the date of their appearance. The 209 cases of typhlitis and perityphlitis give a more satisfactory result.

(p. 123) Dulness was first noticed on the

	Appendicitis	Typhlitis & Perityphlitis
1st day in.....	0 cases	2 cases
2nd " ".....	2 "	0 "
3rd " ".....	1 "	7 "
4th " ".....	4 "	5 "
5th " ".....	1 "	2 "
6th " ".....	2 "	0 "
7th " ".....	1 "	1 "
8th " ".....	1 "	4 "
9th " ".....	0 "	1 "
10th " ".....	0 "	3 "
Total.....	12 cases	25 cases

Palpation showed the presence of the tumor on the

	Appendicitis	Typhlitis & Perityphlitis
1st day in.....	1 case	4 cases
2nd " ".....	3 "	6 "
3rd " ".....	4 "	8 "
4th " ".....	2 "	8 "
5th " ".....	4 "	3 "
6th " ".....	5 "	6 "
7th " ".....	4 "	4 "
8th " ".....	1 "	7 "
9th " ".....	0 "	11 "
10th " ".....	0 "	11 "
Total.....	24 cases	68 cases

An attempt has been made to determine the date at which fluctuation becomes evident. As a rule, its appearance is so late in the course of the disease (after the second week) as to be of little diagnostic value. An exploratory puncture with the needle of the aspirator is frequently recommended to determine the nature of the tumor. Too much stress is not to be laid upon this method of examination. If the aspirator fails to show the presence of pus, even after repeated punctures in divers spots, it by no means follows that pus is absent. Operators have frequently exposed the transversalis fascia over the tumor, and have then punctured it in several places. Pus not appearing, the wound has been dressed. In the course of a few hours an

abundant discharge of fetid matter has made its appearance in the dressings and at the bottom of the wound.

It is evident, from the consideration of the above table, that the (p. 124) presence of the abscess may be expected as early as the third day. It may be large enough to contain some three pints of fluid on the fifth day. The following case reported by Peckham¹ apparently justifies the above conclusions.

His patient was a man twenty-seven years of age, who had suffered from abdominal pain and diarrhoea for twenty-four hours. He was then seized with a severe pain in the right iliac fossa, which was fuller than the left, tender, and dull. On the following day the whole abdomen was tender, but there was no complaint of pain. The day after there were great tenderness, dyspnoea, cold hands and feet. The next day, the fifth of the disease, and the fourth from the occurrence of the right iliac pain, the patient died. There was acute peritonitis. In the lower part of the abdomen was a space bounded by the bladder, iliac bones and small intestine, the latter pushed up and covered by false membrane. In the cavity were nearly three pints of fetid, purulent fluid.

The chief danger from the appendicular peritonitis is that it becomes general. Many of the records mention the time of occurrence, not only of the iliac pain, but also of the subsequent general abdominal pain. The latter is to be regarded as suggestive evidence of the beginning of a general peritonitis, as the former calls immediate attention to the exact nature of the disease. The date of its occurrence is recorded in about one-fourth of the cases of appendicitis, most of which were fatal, while it is noted in but about one-tenth of the cases of typhlitis and perityphlitis, which were nearly all instances of recovery.

General abdominal pain was present on the

	Appendicitis	Typhlitis & Perityphlitis
1st day.....	2 cases	0 cases
2nd ".....	11 "	6 "
3rd ".....	21 "	8 "
4th ".....	12 "	4 "

¹ Boston Med. and Surg. Journ., 106: 159, 1882.

	Appendicitis	Typhlitis & Perityphlitis
5th day.....	8 cases	0 cases
6th "	5 "	1 "
7th "	4 "	0 "
8th "	4 "	0 "
9th "	2 "	0 "
10th "	3 "	0 "
	<hr/> 72 cases	<hr/> 19 cases

(p. 125) In one of the cases in which this symptom appeared on the first day death occurred on the fourth day. It was stated that there was no perforation of the appendix, although this structure presented a deep purple color and contained a fecal concretion. General peritonitis was present and a considerable quantity of pus was found in the pelvis and vicinity of the appendix. In the other case the general abdominal pain came on three hours after moderate pain in the bowels. It radiated from the right iliac region. In sixty-six hours the patient was dead. The intestines were glued together by a butter-like lymph, but there was no serous or seropurulent exudation.

It was thought desirable to ascertain the date at which tympanitic distention of the abdomen appeared. At the same time it is recognized that this sign of a general peritonitis is of considerably less value than that already stated.

Tympanites was present on the

	Appendicitis	Typhlitis & Perityphlitis
1st day.....	0 cases	1 case
2nd "	7 "	5 cases
3rd "	13 "	8 "
4th "	14 "	2 "
5th "	3 "	2 "
6th "	1 "	1 case
	<hr/> 38 cases	<hr/> 19 cases

It is evident, from the above tables, that the majority of cases of resulting general peritonitis begin on the second, third, and fourth days after the inflammation of the appendix is established. This is inferred from the date of the occurrence of the general abdominal pain in sixty per cent of the cases of appendicitis,

and from that of tympanites in nearly ninety per cent of these cases. The source of this early peritonitis is to be found, in most instances, in the escape into the peritoneal cavity of the inflammatory product encysted near the appendix. Although usually small in quantity at this early period, its quality is exceedingly acrid.

The speedy death of the patient almost invariably results from the occurrence of the general peritonitis. In 176 cases the day of death was as follows:

On the	2d	day	in	8	cases	=	4	per	cent.	
" "	3d	" "	" "	20	"	=	11	"	"	
" "	4th	" "	" "	12	"	=	7	"	"	
" "	5th	" "	" "	20	"	=	11	"	"	
" "	6th	" "	" "	16	"	=	9	"	"	
" "	7th	" "	" "	22	"	=	12	"	"	
										(98 in the 1st week, 56 per cent.)
" "	8th	" "	" "	21	"	=	12	"	"	
" "	9th	" "	" "	10	"	=	6	"	"	
" "	10th	" "	" "	8	"	=	4	"	"	
" "	11th	" "	" "	6	"	=	3	"	"	
" "	12th	" "	" "	4	"	=	2	"	"	
" "	13th	" "	" "	4	"	=	2	"	"	
										(54 in the 2d week, 31 per cent.)
" "	14th	" "	" "	1	"					
" "	15th	" "	" "	3	"					
" "	17th	" "	" "	1	"					
" "	18th	" "	" "	1	"					
" "	19th	" "	" "	1	"					
" "	20th	" "	" "	2	"					
										(8 in the 3d week, 4 per cent.)

In the 4th week 7 cases = 4 per cent.

" "	5th	"	4	"	=	2	"	"
" "	7th	"	4	"	=	2	"	"
" "	8th	"	1	"	=	$\frac{1}{2}$	"	"

In fatal cases sixty-eight per cent, more than two-thirds, die during the first eight days, and two-thirds of these die between the fourth and eighth days inclusive.

Errors in the diagnosis of appendicitis have been numerous, chiefly because the cardinal symptoms of localized pain, general heat, and circumscribed swelling have not been duly appreciated in their defined sequence. Again, the extreme rarity of acute perforating inflammation of the caecum, as compared with that

of the appendix, has not been made sufficiently conspicuous. The acute form of perforating appendicitis has been confounded with inflammation of the caecum or typhlitis in an exact sense, intestinal obstruction from intussusception or strangulation, pelvic peritonitis (haematocele) of vesical, ovarian, tubal, or uterine origin, psoriasis, and renal or biliary colic. More rarely a movable kidney or a foreign body in the bladder has been suspected.

The chronic appendicular peritonitis and the chronic paratyphlitis resulting from a perforating appendix have been confounded with the results of caries of the spine and hip-joint, suppurative nephritis, intestinal tuberculosis, and cancer of the caecum. An appreciation of the (p. 127) previous history of the patient, the seat and character of the pain, the period of occurrence of the fever, and the date of the appearance of the tumor are necessary for an eliminative diagnosis.

A primary perforating inflammation of the caecum is extremely rare even in chronic dysentery or in chronic tuberculosis. In an extensive research into the literature of the subject but three cases of acute primary perforation of the caecum have been found: one from a fishbone, another from a pin, and the third from strangulation of the bowel. Two cases of rupture of the caecum are recorded. So rare is the affection in question that the possibility of a primitive, perforating caecitis may be disregarded. Bartholow's¹ communication on this subject relates rather to the secondary perforation of the caecum from without.

Stercoral caecitis, on the contrary, is exceedingly common, and is, perhaps, the most important of all the conditions with which the perforating appendicitis may be confounded. The history of this affection usually makes evident a period of protracted constipation in a person not especially young, vigorous, and apparently healthy, who may have had similar attacks. The pain is trifling for a long time, and the sensitiveness slight. Fever is absent, or of late occurrence. The tumor is present at the beginning as a distinct nodular or doughy mass, elongated, and in the lumbar region. It is unnecessary to say that from a stercoral caecitis may arise a perforative appendicitis which

¹ American Journal of the Medical Sciences, n.s. 52: 351, 1866.

may end in perforation. Many of the so-called cases of typhlitis terminating in resolution, associated with fecal retention, and persisting after the removal of the feces, are undoubtedly of this nature.

Intestinal obstruction from intussusception or strangulation is characterized by the frequent absence of a suggestive previous history. The pain is not so localized or intense, and the fever is not conspicuous at an early stage. The abdomen is distended and tympanitic at the outset, and is, at the same time, unusually sensitive. Borborygmus and perceptible movements of the intestine are associated with or followed by fecal vomiting. Obstinate constipation and the retention of flatus are noticeable. The tumor is absent when the intestine is strangulated, and it is elongated, sausage-like, usually following the course of the colon when intussusception is present. Tenesmus and (p. 128) the rectal discharge of bloody mucus are important signs of the latter affection, though they may occur when the appendix is inflamed.

As four-fifths of the cases of appendicitis occur in males, and as pelvic peritonitis suggests a doubt as to its diagnosis almost invariably in females, it is evident that the question of sex is of eliminative value in certain cases. But the doubt may arise in the case of the female. Barker¹ has reported two cases, the one of haematocele, fatal in forty-eight hours, diagnosed as inflammation of the appendix. The second patient also died on the second day; the autopsy showed an inflamed appendix and pregnancy, although the patient was supposed to have had a haematocele. Suppressed catamenia and the incipient symptoms of appendicitis not infrequently coexist. Again, the occurrence of symptoms of appendicitis within twenty-four hours after delivery is occasional, and more rarely it represents a cause of abortion. In general, the symptoms and progress of a pelvic peritonitis of pelvic origin would not be likely to suggest an inflamed appendix. The symptom which is of the greatest value in determining the onset of an appendicitis after delivery, is to be found in the rapid development of the tumor without an

¹ New York Medical Record, 18: 663, 1880.

obvious cause. When the appendicular peritonitis is pelvic in its localization, the previous history and the absence of evidence of disease of the genital tract are to be relied upon to direct attention to the appendix as the cause.

An inflammation of the psoas muscle may be the result of an appendicitis. If due to other causes, and acute in character, the digestive disturbance is lacking, and the pain and sensitiveness are less, the tumor is more vaguely defined and tympanitic from its deep seat, while the motion of the leg is early impaired. A primary, acute suppurative process is of doubtful occurrence.

A biliary colic is rarely likely to suggest an inflamed appendix. The seat and nature of the pain, the absence of fever and peritonitis during the first week, and the possible occurrence of jaundice would tend to eliminate this affection.

In the passage of a renal calculus the seat and character of the pain differ. Fever and the iliac pain are absent. There is no iliac tumor, and the examination of the urine may indicate the probable presence of a foreign body in the ureter.

(p. 129) In chronic cases of inflamed appendix the abscess is evident, and its treatment apparent. It may be mistaken for a psoas abscess of spinal origin. If the latter affection is present, evidence of disease of the vertebrae is usually to be obtained. In disease of the hip-joint the impaired mobility and localized sensitiveness of this articulation will be found more extreme than is apparent in the flexed and adducted thigh usually connected with a chronic perityphlitic abscess.

The histories of the cases of intestinal tuberculosis, chronic suppurative nephritis, and cancer of the caecum are sufficient to eliminate these causes of iliac and lumbar tumors, when disease of the appendix is under consideration.

Perforating inflammation of the appendix sometimes proves fatal from shock. Death usually follows from the production of a general peritonitis by the direct extension of an appendicular peritonitis, or by the rupture of adhesions producing an intervening, encysted, peritoneal abscess. A general peritonitis may also occur by the intervention of a mesenteric thrombophlebitis

and its continuance to the portal vein and liver, with or without portal embolism. Among the 257 cases of perforating appendicitis are 11 of pylephlebitis.

In the protracted cases death may result from exhaustion. Shock proves fatal within the first two days, death from an extended peritonitis within the first week, and from a secondary general peritonitis, as a rule, during the first two weeks.

The termination in resolution of a perforating appendicitis undoubtedly occurs, but our present sources of information give no absolute evidence as to the relative proportion of this class of cases to those ending fatally. The consideration of a large number of cases of typhlitis and perityphlitis offers a suggestion as to the possible frequency. Of 180 cases thus designated there terminated

By resolution.....	58 = 32 per cent
Spontaneous evacuation.....	33 = 18 " "
Operation.....	89 = 50 " "
	<hr/> 180

It will be generally admitted that the spontaneous evacuation of a perityphlitic abscess is an event to be anticipated and guarded against. Apart from the consequent dangers which may result, possible fatal complications which may precede the time of its expected occurrence (p. 130) are a sufficient warning. It is, therefore, important to bear in mind that two-thirds of the cases of typhlitis and perityphlitis above tabulated were of unquestioned abscess.

The termination by resolution of nearly one-third may seem a sufficient warranty for recognizing this result as frequent enough to be anticipated in all cases.

That this conclusion is not justified appears from the fact that twelve of these, about one-fifth of the entire number, thus terminated at the end of the second week. Operative interference is demanded before this time in two-thirds of all cases, hence but one-fourth may be expected to undergo resolution.

An additional argument against the plan of waiting with the hope of the occurrence of resolution, is to be found in the fre-

quency of recurrent attacks. Recurrence is recorded to have taken place in 28 out of 257 cases of appendicitis, and in 23 out of 209 cases of typhlitis and perityphlitis; that is, in about 11 per cent of each. It is at least suggestive of the importance of not waiting too long for resolution, that the number thus terminating during the last two days of the second week is seven per cent of those ending in resolution. This number may include a considerable part of the recurrent cases which operative interference would have prevented.

The possibility of a termination by resolution must be recognized, and the earliest therapeutic efforts should have this result in view; especially as these efforts also tend toward localizing the peritonitis. But, as Pepper¹ states, "the unjustifiable delay permitted in many cases of typhlitis, whilst hoping day after day for the more definite detection of suppuration, is the direct cause of many avoidable deaths."

To keep the bowels quiet should be the first and last thought. Absolute rest in bed, liquid diet in small quantities often repeated, and, above all, sufficient opium to neutralize pain. A sufficiency may seem enormous. Pétrequin² gave a grain of opium every hour till the pain was relieved, with the result of administering 107 grains in six days. Clark³ gave a boy, fourteen years old, 1350 drops of laudanum in one day.

A cathartic or a laxative may be demanded by the patient or friends, and an enema be thought desirable as a diagnostic aid. It is to be (p. 131) remembered that these may be the means of at once exciting a general peritonitis. With⁴ states that in the milder cases the pain disappears in a few days, vomiting ceases, and within five or six days tenderness and distention disappear. The bowels open spontaneously a few days after the discontinuance of the opium. They may remain bound for twenty-four days, yet the general health need not suffer. Recovery may proceed quietly, steadily, and without disturbance, and the appetite return long before the bowels are opened.

¹ Ext. Trans. Med. Soc. of Penna, 1883.

² Gaz. Méd. de Paris, 2me S.: 438, 1837.

³ Amer. Med. Times, 3: 258, 1861.

⁴ Loc. cit.

If, after the first twenty-four hours from the onset of the severe pain, the peritonitis is evidently spreading, and the condition of the patient is grave, the question should be entertained of an immediate operation for exposing the appendix and determining its condition with reference to its removal. If any good results are to arise from such treatment it must be applied early. Burchard¹ is an enthusiastic advocate of "lumbar typhlotomy in acute perforating typhlitis." No surgeon would hesitate to give this additional chance for life were he satisfied that perforation had actually occurred, and a general peritonitis was imminent.

If surgical interference is not instituted within the first twenty-four hours after the onset of the sudden and intense right iliac pain, to keep the bowels quiet must still be the injunction. The formation of the tumor, the circumscribing of the peritonitis, is then to be awaited. It is sure to form, in the large majority of cases, if the patient lives long enough. It is only in a small fraction that it occurs before the third day. In more than two-thirds of the cases the contents will escape externally or internally. Without surgical aid the escape is into the peritoneal cavity in most instances, with a rapidly fatal result. In a smaller number the escape elsewhere not infrequently produces serious if not fatal sequels.

Iliac abscesses were sometimes incised before the days of Dupuytren and Grisolle.² The latter writer recommended that they should be opened as soon as fluctuation could be detected, in opposition to the generally prevailing view that nature should take its course. It was left to Mr. Hancock,³ however, to operate before this sign could be recognized. He advocated incision into the tumor in certain stages and forms of mischief, resulting from the presence of impacted feces or (p. 132) foreign substances, in either the caecum or its appendix, which have hitherto, for the most part, invariably proved fatal. He contended that the typhoid condition into which patients affected with peritoneal

¹ N. Y. Med. Journ., 33: 1, 1881.

² Arch. Gén. de Méd., 4: 314, 1839.

³ London Med. Gaz., n.s. 7: 547, 1848.

inflammation fell, did not depend upon the violence of the disease, but upon the effused fluid, the removal of which he thought the only chance of saving the patient. His reasons for operating in the given cases are thus stated: "As she was evidently sinking, and the previous treatment had been of no avail, I proposed to make an incision from the spine of the ilium to the inner side of the internal abdominal ring over the hardened spot, so that if it were intestine or omentum it could be freed, or if, as was thought more probable, matter had collected in the right iliac fossa, it could be let out, and thus give our patient a chance for recovery."

Some years later Lewis¹ contributed a paper on abscess of the appendix, which included an abstract of forty-seven cases, only one of which recovered. He referred to Hancock's communication, and urged the propriety of opening the tumor in case of threatening urgency even if fluctuation were absent. Willard Parker,² however, deserves the credit of having demonstrated the success of this operation in three out of four cases, and it is his advocacy of an early operation which has produced such favorable results since 1867. He thought surgery useless in the absence of adhesions, but opportune after the fifth day, when their presence is probable, and the fear of rupture imminent. He considered that an incision made between the fifth and twelfth days was practicable, safe, and justifiable. Even when the diagnosis was doubtful, "if no abscess had already formed, in case one should be in process of formation, an external opening would tend to make it point in a safe direction; and if no abscess should form a free incision would relieve tension, thus adding to the comfort of the patient, and in no way prejudicing his safety."

In 1873, W. T. Bull³ published an admirable paper on perityphlitis, based upon an analysis of sixty-seven cases thus designated. Thirty-two, nearly forty-eight per cent, terminated fatally, and in fifteen of these there was perforation of the appendix. Noyes,⁴ in 1882, collected a series of one hundred cases

¹ N. Y. Journ. of Med., 1: 328, 1856.

² N. Y. Med. Record, 2: 25, 1867.

³ N. Y. Med. Journ., 18: 240, 1873.

⁴ Reprint from Trans. R. I. Med. Soc. for 1882-83.

of perityphlitis treated by operation, of which eighty were published after the appearance of Parker's (p. 133) paper. Of these, fifteen died, fifteen per cent of the whole. Even this greatly lowered mortality might have been diminished by excluding one case of cancer and another of phthisis. The almost invariable fatality, in Mr. Hancock's time, of cases not terminating in resolution has thus been reduced to less than fifteen per cent by the general acceptance of a given operation under definite conditions.

In the table¹ which has been prepared to show the day of death in cases of perforating appendicitis, it appears that 60 out of 176 cases, or 34 per cent, died during the first five days. This early mortality is sufficiently explained by the consideration of the table² of symptoms indicating the onset of a general peritonitis. It appears that of 73 cases of general abdominal pain, this symptom appeared during the first five days in 54 instances, or 74 per cent. Tympanites was noticed during the first period in 37 out of 38 cases, or 97 per cent. It is thus evident that the earliest date fixed by Dr. Parker is too late to afford the possibility of relief in more than one-fourth of all the cases. But early as this date may seem, it has almost universally been the custom to postpone the time of operating till later in the course of the disease. The following table is based upon the analysis of 87 cases of typhlitis and perityphlitis. The operation was performed:

On the	3d	day in	1 case	} 8 = 9 per cent.
" "	5th	" "	1 "	
" "	6th	" "	3 cases	
" "	7th	" "	3 "	
" "	8th	" "	7 "	} 41 = 47 per cent.
" "	9th	" "	3 "	
" "	10th	" "	11 "	
" "	11th	" "	4 "	
" "	12th	" "	4 "	
" "	13th	" "	6 "	
" "	14th	" "	6 "	

¹ Page 126.

² Page 124.

On the 15th day in	5 cases	} 15 = 17 per cent.
" " 17th " "	4 "	
" " 18th " "	2 "	
" " 19th " "	1 case	
" " 20th " "	3 cases	
After 3d week		$\frac{23}{87} = 26 \text{ per cent.}$

(p. 134) Hence if the indications for operating justified the election of a date as early as the fifth day, they still more justify the choice of the third day.

The result has shown the wisdom of the former step, and the evidence here presented seems not only to warrant, but to demand the latter. It is evident that the operation to be performed is that of opening the abdominal cavity. It is, therefore, unnecessary to state that an act which twenty years ago might have added to the risks of the patient, may at the present time, when properly performed, be confidently expected to reduce them very materially.

That the incision of the tumor, in cases of perityphlitis, is even now frequently omitted, is apparent from the consideration of the cases of inflamed appendix recently recorded. Of 57 cases occurring, for the most part, during the past five years, there were signs of a tumor in 16; an operation was performed in only 7. The tumor was opened in 4 cases, twice successfully. Laparotomy was performed as a last resort in 3 instances, the diagnosis being intestinal obstruction: the cause of the peritonitis was not discovered, and death speedily followed.

Notwithstanding this evidence of a fatal delay in the appropriate treatment of cases of appendicitis, the tendency to the performance of an earlier operation is growing. Bull¹ states that he operated on the third day after the patient was seized with chill, fever, vomiting, and constipation. There were severe right iliac pain and increased resistance on pressure. The aspirator showed pus in the lumbar region, and an abscess was opened behind the colon. Death occurred two days later, and the autopsy showed a perforated appendix, paratyphlitis, and general peritonitis.

¹N. Y. Med. Record, 29: 267, 1886.

Barlow and Godlee¹ made an exploratory incision in the median line on the fifth day. They found early general peritonitis and lymph near the caecum surrounding a collection of fetid pus, presumably of appendicular origin. A second incision was made over the latter. Recovery took place.

Homans² operated successfully on the sixth day of the disease, probably perforation of the appendix, and the second day after the patient was seen by his physician, Dr. Greene, of Dorchester. The incision (p. 135) was made into the abdominal cavity over the seat of pain. The adherent intestines were separated, and some two ounces of pus removed.

Keen³ also operated on the sixth day after the occurrence of sudden, intense, right iliac pain. Although the symptoms had been characteristic, they were abating. There was increased resistance, however, dulness on deep pressure, a doughy sensation, and considerable oedema in the right iliac fossa. The aspirator showed pus, and a pint was removed after the abscess was opened.

The presence of a general peritonitis does not contraindicate the operation. The case of Barlow and Godlee shows that the general peritonitis may have begun yet the patient recover. Treves⁴ operated upon a case of peritonitis of two days duration, supervening upon an attack of pelvic peritonitis of some three months' standing. The patient recovered. Mikulicz⁵ operated on the sixth day after the sudden right iliac pain in a case where there was evidence of rupture of the abscess into the general peritoneal cavity on the fourth day. The wound was closed, slight improvement followed, but death occurred on the eleventh day.

If the encysted peritonitis becomes general, death has heretofore been almost inevitable. It is thus obvious that if laparotomy was successful in two out of three cases where a secondary general peritonitis was present, there is more than a chance of recovery by its use even in hitherto necessarily fatal cases. But

¹ *Med. Times & Gazette*, 2: 852, 1885.

² *Boston Med. & Surg. Journ.*, 114: 388, 1886.

³ *Med. & Sur. Reporter*, 54: 165, 1886.

⁴ *Medico-Chirurgical Transactions*, 2 s., 1: 175, 1885.

⁵ *Volkmann's Samml. klin. Vortr.*, 262: 2313, 1885.

it should be employed only when suitable, and not as a last resort when patients are moribund.

In conclusion, the following statements seem warranted:

The vital importance of the early recognition of perforating appendicitis is unmistakable.

Its diagnosis, in most cases, is comparatively easy.

Its eventual treatment by laparotomy is generally indispensable.

Urgent symptoms demand immediate exposure of the perforated appendix, after recovery from the shock, and its treatment according to surgical principles.

If delay seems warranted, the resulting abscess, as a rule intraperitoneal, should be incised as soon as it becomes evident. This is usually on the third day after the appearance of the first characteristic symptom of the disease.

THE END



CHARLES MCBURNEY

American Journal of Surgery, N.S. 11, February, 1931



Charles McBurney

BIOGRAPHY

- 1845 Born Feb. 17, in Roxbury, now part of Boston, Mass. of paternal Scotch-Irish and maternal New England ancestry. Received early education in Roxbury Latin School and in private schools of Boston.
- 1862 Age 17. Entered Harvard University.
- 1866 Age 21. Received degree Bachelor of Arts from Harvard.
- 1869 Age 24. Master of Arts at Harvard.
- 1870 Age 25. Doctor of Medicine from College of Physicians and Surgeons, New York City.
- 1871 Age 26. Surgical internship of 18 months at Bellevue Hospital, New York. Rowed almost daily on East River in single shell. Then took postgraduate study in Europe.
- 1873 Age 28. Began practice in New York, associated with Dr. George A. Peters. Assistant demonstrator of anatomy at College of Physicians and Surgeons under Dr. Henry B. Sands.
- 1875 Age 30. Attending surgeon, St. Luke's Hospital. Married Mary Willoughby Weston, Oct. 8, the union being blessed by 2 sons and 1 daughter.
- 1878 Age 33. Lecturer on Anatomy of Nerves until 1880.
- 1880 Age 35. Assistant surgeon, Bellevue Hospital.
- 1882 Age 37. Lecturer on operative surgery, College of Physicians and Surgeons until 1889.
- 1886 Age 41. Consulting surgeon to Presbyterian Hospital, New York Hospital and Hospital for Ruptured and Crippled.

- 1888 Age 43. Given entire surgical service of Roosevelt Hospital. Held position for 12 years, working in Sims' amphitheatre, a mecca for surgeons from all over the world.
- 1889 Age 44. Professor of surgery, College of Physicians and Surgeons until 1894. Described point of maximal tenderness of abdomen in acute appendicitis (McBurney's point).
- 1892 Age 47. Vice-president, New York Academy of Medicine. Honorary member of College of Physicians and Surgeons of England. Honorary member of College of Physicians and Surgeons of Philadelphia.
- 1894 Age 49. Professor of clinical surgery at College of Physicians and Surgeons. Proposed new incision for appendectomy (McBurney's incision).
- 1908 Age 63. Retired because of ill health.
- 1913 Age 68. Died Nov. 7, at home of sister in Brookline, Mass., of heart failure following a hunting trip to Maine. Was an ardent devotee to golf, an expert shot and salmon fisherman.

Also consulting surgeon to New York, Presbyterian, Orthopedic, St. Mark's, St. Luke's, Ruptured and Crippled Hospitals.

Was also member of New York Surgical Society, Practitioner's Society, Roman Medical Society, Fellow of Royal College of Surgeons of Edinburgh, a corresponding member of the Société de Chirurgie of Paris, an honorary member of the Medical Society of Constantinople.

EPONYMS

1. INCISION: Muscle splitting or gridiron. *The incision made in the abdominal wall in cases of appendicitis, with a description of a new method of operating.* Ann. Surg., 20: 38-43, 1894.
2. MANEUVER: Reduction with hooks of the dislocated head of the humerus in fracture of surgical or anatomical neck; also called C. B. Porter hook maneuver. *Dislocation of the humerus complicated by fracture at or near the surgical neck,*

with a new method of reduction. Ann. Surg., 19: 399-415, 1894.

3. OPERATION: For the radical cure of inguinal hernia; the sac is exposed, ligated, and cut off at the internal ring; the skin is turned in and stitched to the underlying tendinous and ligamentous structures. *The radical cure of hernia, with special reference to open treatment of the operation wound.* N. Y. Med. Jour., 47: 57, 1888.
4. POINT: The point of special tenderness in appendicitis: between an inch and a half and two inches from the anterior spinous process of the ilium on a straight line drawn from that process to the umbilicus. *Experience with early operative interference in cases of disease of the vermiform appendix.* N. Y. Med. Jour., 50: 676-684, 1889.

BIBLIOGRAPHY OF WRITINGS

1. Fistula in the anterior portion of the urethra. Med. Rec., 21: 244, 1882. Also: Illust. Quart. M. & W., N. Y., 1: 59-65, 1882.
2. Acute osteomyelitis following slight injury of the ankle. Med. News, 42: 721, 1883.
3. Tracheotomy as a preliminary to certain operations. Ibid., 136-139. Also: N. Y. Med. Jour., 37: 326-329, 1883. Also: Ann. Anat. & Surg., 7: 201-207, 1883.
4. Compound comminuted fracture of the skull; absence of brain symptoms; healing by first intention; recovery. Med. News, 43: 637, 1883. Also: N. Y. Med. Jour., 38: 610, 1883.
5. Excision of the elbow. Med. News, 45: 721, 1884.
6. Aneurism of the femoral artery; ligation of the external iliac; cure. N. Y. Med. Jour., 39: 251, 1884.
7. Epithelioma of the larynx. Ibid., 371.
8. Cases of knee joint excision. Ibid., 381; 391. Also: Med. News, 44: 409-412; 424, 1884.
9. Excision of the knee joint. N. Y. Med. Jour., 41: 421, 1885. Also: Med. News, 46: 415-417, 1885.
10. Congenital angioma. N. Y. Med. Jour., 42: 555, 1885.

11. Two cases of operation for pyloric stenosis. *Ibid.*, 43: 78-80, 1886. Also: *Med. News*, 48: 58-62, 1886. Also: *Ann. Surg.*, 3: 372-380, 1886.
12. Orbital aneurysm. *N. Y. Med. Jour.*, 43: 333, 1886.
13. Fibro-sarcoma of the medial nerve. *Ibid.*, 504.
14. Szymanowski's operation as applied to the cure of urethro-perineal fistula. *Ann. Surg.*, 4: 461-467, 1886.
15. Case of aneurysm of the innominate artery treated by ligature of the carotid and subclavian. *N. Y. Med. Jour.*, 45: 191, 1887.
16. Excision of the ankle joint. *Ibid.*
17. Right inguinal hernia with non-descent of the testis; castration. *Med. News*, 1: 613, 1887.
18. Hernia of right ovary; successful removal of gland. *Ibid.*
19. The radical cure of hernia, with special reference to open treatment of the operation wound. *N. Y. Med. Jour.*, 47: 57-61, 1888.
20. Septic peritonitis following perforation of the vermiform appendix. *Ibid.*, 719-721.
21. Case of traumatic rupture of kidney. *Times & Reg.*, *Phila.*, 20: 772, 1889.
22. Experience with early operative interference in cases of disease of the vermiform appendix. *N. Y. Med. Jour.*, 50: 676-684, 1889.
23. Contusion of the abdomen with extensive hemorrhage; laparotomy; recovery. *Ibid.*, 49: 106.
24. The radical cure of inguinal hernia. *Med. Rec.*, 35: 312-318, 1889. Also ref.: *Med. News*, 54: 245-247, 1889.
25. Carcinoma of rectum. *N. Y. Med. Jour.*, 49: 355, 1889.
26. Extirpation of thyroid gland. *Ibid.*, 444.
27. Thiersch's method of skin-grafting. *Ibid.*, 52: 442-444, 1890. Also: *Med. News*, 56: 427, 1890. Also: *Med. Rec.*, 38: 453-456, 1890. Also: *Trans. N. Y. Acad. Med.*, 1890, 2. s., 7: 317-331, 1891.
28. Double hydrocele. *Med. News*, 56: 342, 1890.
29. Chronic abscess of femur. *Ibid.*
30. Radical cure of inguinal hernia (abstract). *Ibid.*, 343.

31. Trephining of skull for epilepsy. *Ibid.*, 479.
32. Excision of a spina bifida. *Ibid.*
33. Excision of a branchiogenic cyst. *Ibid.*, 57: 38.
34. Acute appendicitis. *N. Y. Med. Jour.*, 52: 329, 1890.
35. Recurrent appendicitis. *Ibid.*
36. Osteosarcoma of the left scapula; tumor of thyroid gland; Thiersch's method of skin-grafting. *Internat. Jour. Surg.*, 3: 286, 1890.
37. Suprapubic section. *N. Y. Med. Jour.*, 53: 309, 1891.
38. The indications for early laparotomy in appendicitis. *Ann. Surg.*, 13: 233-254, 1891.
39. Trephining for traumatic aphasia; recovery. *N. Y. Med. Jour.*, 53: 517, 1891.
40. Section of the intestine for removal of gall-stone. *Ibid.*, 520.
41. Discussion on appendicitis; indications for early operation. *Trans. Med. Soc. N. Y.*, p. 208, 1891.
42. Contribution to Dennis' System of Surgery.
43. Contribution to International Textbook of Surgery.
44. Traumatic hemorrhage from a vein of the pia mater; compression of Broca's convolution and of the sensorimotor area of the cortex; aphasia; partial hemiplegia and hemianesthesia; trephining; removal of clot; recovery. With Starr, M. A. *Brain*, London, 14: 284-288, 1891.
45. Cases of appendicitis, illustrating different forms of the disease. *Med. Rec.*, 41: 421-427, 1892. Also: *Trans. N. Y. Acad. Med.*, 1892, 2. s., 9: 79-109, 1893.
46. Osteoplastic resection of the upper jaw for nasopharyngeal polypus. *N. Y. Med. Jour.*, 55: 580, 1892.
47. Osteosarcoma of the jaw. *Ibid.*
48. Traumatic epilepsy, operated upon. *Med. & Surg. Reporter*, 66: 881, 1892.
49. Trephining for cranial injury. *Med. Rec.*, 42: 742, 1892.
50. Fibrosarcoma of cerebellum and pons. With Starr, M. A. *Ibid.*, 43: 87.
51. Glioma of cerebellum. *Ibid.*, 88.
52. The treatment of general septic peritonitis due to appendicitis. *Ann. Surg.*, 18: 42-48, 1893.

53. A contribution to cerebral surgery. Diagnosis, localization, and operation for removal of three tumors of brain; with some comments upon the surgical treatment of brain tumors. With Starr, M. A. *Am. Jour. Med. Sc.*, n.s., 105: 381-387, 1893. Also: 22 pp., 8°, Phila., 1893.
54. The incision made in the abdominal wall in cases of appendicitis, with a description of a new method of operating. *Ann. Surg.*, 20: 38-43, 1894.
55. Cyst of the pancreas. *Ibid.*, 19: 492.
56. Dislocation of the humerus complicated by fracture at or near the surgical neck, with a new method of reduction. With Dowd, C. N., *Ibid.*, 399-415; 493-497. Also: 17 pp., 8°, Phila., 1894.
57. Cases illustrating the use of a mechanical appliance to correct the deformity after removal of half of the lower jaw. *Ann. Surg.*, 20: 35-37, 3 pl., 1894.
58. Sarcoma of kidney. *Ibid.*, 373-376.
59. Chronic dislocation of shoulder with fracture reduced by hooks. *Ibid.*, 21: 299-301, 1895.
60. Sarcoma of ovary in a girl aged ten years. *Ibid.*, 706.
61. Rupture of quadriceps extensor tendon. *Ibid.*, 22: 506-508.
62. Fracture of the pelvis. *Trans. Amer. Surg. Assn.*, 13: 503-505, 1895.
63. Epithelioma of the tonsil. *Ibid.*, 505.
64. Traumatic popliteal aneurysm. *Ibid.*, 506.
65. Sarcoma of radius. *Ibid.*
66. Suture of quadriceps tendon. *Ibid.*, 507.
67. Removal of the lower jaw. *Ibid.*, 508.
68. Appendicitis. *Ibid.*
69. Treatment of the diffuse form of septic peritonitis occurring as a result of appendicitis, with cases. *Med. Rec.*, 47: 385-390, 1895.
70. Fracture of the humerus associated with dislocation of the shoulder joint. *N. Y. Polyclin.*, 5: 72-75, 1895.
71. Carcinoma of breast. *Med. News*, 68: 269, 1896.
72. Acute appendicitis. *Ibid.*, 270.
73. The treatment of appendicitis. *Ibid.*, 69: 653-656. Also: 11 pp., 12°, N. Y., 1896.

74. Non-recurrence of sarcoma of naso-pharynx three years after operation. *Med. Rec.*, 49: 204, 1896.
75. Non-recurrence of cancer of tonsil three years after operation. *Ibid.*
76. Surgical treatment of appendicitis. *Dennis' System of Surgery*, 4: 415-433, 1896.
77. Speech at sixth annual dinner of Harvard Medical Alumni Association. *Boston Med. & Surg. Jour.*, 135: 316-322, 1896.
78. The surgery of the future. *Ibid.*, 384.
79. Inguinal hernia and varicocele. *Internat. Jour. Surg.*, 9: 41, 1896.
80. Inguinal hernia, Bassini's operation. *Ibid.*, 43.
81. Separation of the upper epiphysis of humerus; open operation. *Ann. Surg.*, 23: 177-180, 1896.
82. Sarcoma of radius; amputation of forearm by a new method. *Ibid.*, 181-183.
83. Nephrectomy for displaced kidney and hydronephrosis. *Ibid.*, 183-185.
84. Nephrectomy for abscess of kidney. *Ibid.*, 282.
85. Successful resection of small intestine for sarcoma with intussusception. *Ibid.*, 441-444.
86. Reduction of dislocation of the humerus complicated by fracture at the anatomical neck; operative treatment of separation of the lower epiphysis of the femur. *Ibid.*, 510-519.
87. Operative treatment of carcinoma of the breast. *Ibid.*, 607.
88. Appendicitis obliterans. *Ibid.*, 608.
89. Result of Halsted's operation for carcinoma of breast. *Ibid.*, 25: 363, 1897.
90. Direct intra-abdominal finger compression of the common iliac artery during amputation at the hip joint. *Ibid.*, 610-613; 714.
91. The treatment of appendicitis. *N. Y. Polyclin.*, 9: 1-5, 1897.
92. The surgery of the future. *Semi-Centen. Anesthesia*, Boston, pp. 69-76, 1897.

93. Is not the mortality from surgical disease larger than necessary? *Med. Rec.*, 52: 881; 894-896, 1897. Also: *Canada Lancet*, 30: 328-330, 1897.
94. A case of carcinoma of the tonsil. *Med. Rec.*, 52: 893, 1897.
95. Cancer of the breast. *Internat. Jour. Surg.*, 11: 144, 1898.
96. Cancer of the lip. *Ibid.*, 47.
97. Epithelioma of the lower lip. *Ibid.*, 144.
98. Recurrent appendicitis. *Ibid.*, 308-310.
99. Vesical calculus. *Ibid.*, 145.
100. Aneurism. *Ibid.*, 146.
101. (Superficial sarcoma over right clavicle.) *Ibid.*, 307.
102. (Recurring appendicitis.) *Ibid.*, 308-310.
103. Traumatic rupture of spleen; extirpation. *Med. Rec.*, 53: 601, 1898.
104. Use of rubber gloves in operative surgery. *Ann. Surg.*, 28: 108-119, 1898.
105. Aneurism of the external iliac artery; treated by ligation of common iliac. *Ibid.*, 128.
106. Amputation at hip joint for recurrent sarcoma. *Ibid.*, 129-131.
107. Complete resection of clavicle for osteosarcoma. *Ibid.*, 259.
108. Plastic operation for deformity of nose. *Ibid.*, 258.
109. Removal of biliary calculi from the common duct by the duodenal route. *Ibid.*, 481-486.
110. The technic of aseptic surgery. *Internat. Text-book Surg.*, 1: 263-305, Phila., Warren & Gould, 1899.
111. Recurrent appendicitis; tuberculous disease of the knee joint. *Internat. Jour. Surg.*, 13: 244-246, 1900.
112. Remarks concerning the practice of aseptic surgery. *N. Y. Med. Jour.*, 75: 490-496, 1902.
113. The surgical treatment of hemorrhoids. *Ibid.*, 81: 417-422, 1905.
114. Amputation at hip joint for tuberculosis. (Case report) *Med. Rec.*, 73: 667, 1908.

BIBLIOGRAPHY OF BIOGRAPHIES

- Obituary. *Brit. Med. Jour.*, 2: 1413; 1465, 1913.
 Obituary. *Jour. Amer. Med. Assn.*, 61: 1826, 1913.

- Obituary. *Lancet*, Lond., 2: 1502, 1913.
 Obituary. *Med. Rec.*, 84: 903, 1913.
 Obituary. *Physicians & Surg.*, 35: 521-523, 1913.
 Obituary by Johnson, A. B. *N. Y. Med. Jour.*, 98: 978, 1913.
 Historical sidelights on appendicitis. (Letters from C. McBurney) *Med. Life*, 29: 332-336, 1922.
 Master surgeons of North America: Charles McBurney. By Peck, C. H. *Surg., Gynec. & Obst.*, 36: 430-432, 1923.
 Contributors to the science of medicine: Charles McBurney. *Med. Jour. & Rec.*, 99: 208, 1924.
 Eponym: McBurney's point. *Amer. Jour. Surg.*, 8: 728, 1930.
 McBurney's point, *Ibid.*, 11: 364, 1931.

INDEX TO BIBLIOGRAPHY

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	100, 105	1898
" orbital.....	12	1886
Angioma.....	10	1885
Ankle, excision of.....	16	1887
Aphasia, traumatic.....	39, 44	1891
Appendicitis.....	20	1888
	22	1889
	34, 35	1890
	38, 41	1891
	45	1892
	52	1893
	54	1894
	68, 69	1895
	72, 73,	
	76, 88	1896
	91	1897
	98, 102	1898
	101	1900

	Reference	Year
Branchiogenic cyst.....	33	1890
Breast, carcinoma of.....	71, 87	1896
	89	1897
	95	1898
Calculi, biliary.....	109	1898
" vesical.....	99	1898
Cerebellum, tumors of.....	50, 51	1892
Clavicle, sarcoma of.....	101, 107	1898
Cranial injury.....	49	1892
" surgery.....	53	1893
Elbow, excision of.....	5	1884
Epilepsy.....	31	1890
	48	1892
Femur, abscess of.....	29	1890
Gall-stone in intestine.....	40	1891
Hemorrhoids.....	113	1905
Hernia, inguinal.....	17	1887
	19	1888
	24	1889
	30	1890
	79, 80	1896
Hip joint, amputation of.....	90	1897
	106	1898
	114	1908
Humerus, fracture and dislocation of.....	56	1894
	58, 70	1895
	81, 86	1896
Hydrocele.....	28	1890
Intestine, sarcoma of.....	85	1896
Jaw, operation on.....	57	1894
	67	1895
Kidney, abscess of.....	84	1896
" rupture of.....	21	1889
" sarcoma of.....	58	1894
" surgery of.....	83	1896
Knee, excision of.....	8	1884
	9	1885

	Reference	Year
Larynx, epithelioma of	7	1884
Lip, cancer of	96, 97	1898
Mortality, surgical	93	1897
Naso-pharynx, sarcoma of	74	1896
Nerve, median	13	1886
Nose, plastic operation on	108	1898
Osteomyelitis	2	1883
Osteosarcoma, of jaw	47	1892
" of scapula	36	1840
Ovary, hernia of	18	1887
" sarcoma of	60	1895
Pancreas, cysts of	55	1894
Pelvis, fracture of	62	1895
Quadriceps extensor, rupture of	61, 66	1895
Radius, sarcoma of	65	1895
	82	1896
Rectum, carcinoma of	25	1889
Rubber gloves in surgery	104	1898
Skin grafting	27, 36	1890
Skull, fracture of	4	1883
Spina bifida	32	1890
Spleen, rupture of	103	1898
Stomach, pyloric stenosis	11	1886
Suprapubic section	37	1891
Surgery, aseptic	110	1899
	112	1902
Szymanowski's operation	14	1886
Thiersch's skin graft	27, 36	1890
Thyroid, operation	26	1889
Tonsil, epithelioma of	63	1895
	75	1896
	94	1897
Tracheotomy	3	1883
Urethral fistula	1	1882
	14	1886
Vesical calculus	99	1898

McBURNNEY'S POINT

One of the mile-stones along the road of revelation of the true nature of appendicitis must bear the name of Charles McBurney. Before him, of course, in time and importance, are the names of Fernal (1554), Hesiter (1711), Mestivier (1759), LaMotte (1766), James Parkinson (1812), Villermay (1824), Melier (1827) and others down to Reginald H. Fitz of Boston who first established the true pathologic process and applied the term appendicitis in 1886. McBurney's first paper on this disease appeared two years later, *Septic peritonitis following perforation of the vermiform appendix*. N. Y. Med. Jour., 47: 719-721, 1888. Every year thereafter for a decade there was at least one paper on appendicitis published by this surgeon who had entire charge of the surgical service at Roosevelt Hospital and was Professor of Surgery in the College of Physicians and Surgeons in New York City.

For recognizing the light given by Fitz, for studying and reporting cases of appendicitis, and for passing on the light to others, posterity has "rewarded" McBurney by attaching his name to one of the most common signs of the disease, a point of tenderness in the right lower abdominal quadrant.

The paper announcing this clinical sign is entitled *Experience with early operative interference in cases of disease of the vermiform appendix*. N. Y. Med. Jour., 50: 676-684, 1889. See the following pages for the complete paper. The author was very specific in locating the point of greatest tenderness, placing it, as "determined by the pressure of one finger,"—"very exactly between an inch and a half and two inches from the anterior spinous process of the ilium on a straight line drawn from that process to the umbilicus."

After McBurney, several other authors brought forth their pet points of maximum tenderness in acute appendicitis, but many of these authors we must accuse of desiring to equivocate or to attract attention. Many writers argue that since the location of the appendix is not fixed, the point of maximum tenderness must vary. However, pain on pressure at McBurney's point is explained by reflexly irritated nerve endings of the eleventh and twelfth dorsal segments on the anterior abdominal wall. The same nerve segment is always irritated so that the point remains

fixed no matter in which direction the diseased appendix may extend.

Many recent authors have incorrectly described the location of McBurney's point. Thus Osler in *Practice of Medicine*, 7th edition, page 515, and 9th edition, page 524, and Dean Lewis in Cecil's *Textbook of Medicine*, 1st edition, page 711, place McBurney's point at the middle of a line joining the umbilicus and right anterior superior spine. Bailey, deQuervain and Sloan do not mention the point at all, much less give it its proper name. Murphy, Rose and Carless, Romanis and Mitchiner, Ashhurst, Da-Costa, Royster, Livingston and Donhauser describe the point correctly.

If we persist in using eponyms in medicine (and we should), our application of them must be limited to the exact condition originally described. Perhaps the unavailability of the original paper has been a large factor in inaccurate reference. To supply these originals is the purpose of this publication.



Experience with Early Operative Interference in Cases of Disease of the Vermiform Appendix

BY

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LVENTURE to introduce once more a subject that has been so ably treated by numerous writers, because I have for some time been devoting my attention in suitable cases to a particular line of treatment, and because I have been fortunate enough to have had recently a considerable number of cases of disease of the appendix under my care. Nearly two years ago the account of a case of successful laparotomy for perforation of the vermiform appendix was read before this society by our much-lamented colleague, Dr. Henry B. Sands. The case was a most brilliant one throughout, and illustrated particularly well the cleverness of diagnosis and the rapidity of successful action which we all remember as so characteristic of the reader of that paper. It should not be forgotten that at that time such action was a very bold step into ground

that was almost unknown. We did not all agree with Dr. Sands in the views which he expressed in regard to the pathology of perityphlitis, but these views did not prevent him, when the proper case occurred, from making, in regard to treatment, a brilliant stride in advance of others. This case gave an impulse to the study of inflammatory affections of the vermiform appendix from which we shall not recover for a long time. During the following months Dr. Sands devoted much attention to this study, and it was my privilege to assist him in a number of successful operations for the removal of the appendix at an early stage of disease. It seemed to me that each one of these operations shed a flood of light upon the pathology of the so-called pericecal inflammations, and during the summer following, while discussing the subject, he expressed to me views which were far in advance of most surgeons and very different from those which he entertained at the time when he wrote his last paper. If he were here to-night he would, by the results of his own last year's original work, enlighten us upon many points respecting the pathology of perityphlitis. I feel it a pleasure and a duty to thus refer to Dr. Sands, because, unfortunately, no special record has been kept of his last year's brilliant work, and his sudden death prevented him from telling us himself what would have been so valuable. Certainly no other surgeon ever did so much to improve the treatment of a very fatal disease. Beginning with the first suggestion of Dr. Willard Parker, which taught surgeons how to save many lives, although by a slow and often unsatisfactory process, Dr. Sands ended his work in this direction by showing us how we might cut short at its very inception a disease that is even to-day responsible for many deaths.

It is not my intention in this paper to attempt to present the subject of pericecal inflammation in a systematic manner. That has already been done, and very recently, by a large number of writers. I have chosen rather to dwell upon some points in the pathology and treatment of these inflammations, which are beginning to be better understood and which especially interest us all. The fact that inflammatory affections of the vermiform appendix give rise to a considerable number of the so-called

pericecal inflammations is now accepted in every part of the medical and surgical world, although one still reads of perityphlitis and paratyphlitis, and of intraperitoneal and extraperitoneal abscesses. Certainly all of these terms are misleading, inasmuch as each of them, when used without explanation, implies that the particular disease to which it refers is a disease by itself, and fundamentally different from the others. The usual term perityphlitis means, strictly speaking, nothing more than an inflammation of the peritoneum surrounding the cecum, but it is understood by many to mean often a localized and harmless peritonitis arising from impaction of feces, by others a fatal septic disease originating in perforation of the appendix. Now it is unquestionably true that every case of inflammation of the appendix is sooner or later accompanied by inflammation of the neighboring peritoneum, either on the cecum or mesentery or ileum, etc., but if from the whole list of acute inflammatory affections occurring in the right iliac fossa we set aside those originating in the appendix, how many shall we have left? Very rarely will occur a perforation of the cecum by ulcer or foreign body, giving rise to a local peritonitis at this point, and traumas from without may accomplish the same result. For all of such causes as compared with inflammations of the appendix, let me hazard the proportion one in one hundred.

How many cases of localized peritonitis or perityphlitis arise from impaction of feces in the cecum? Some writers would lead us to believe that this is a frequent cause, and not long ago it was looked upon as the *most* frequent cause. Is there a *single* observation brought from the dead-house or from the operating-table to support this idea? I have never heard or read of such observation, and I do not believe that any such case ever occurred. Clinically we meet with cases of pain in the right iliac fossa, accompanied by some rise of temperature, and not infrequently in these cases we may detect masses of feces in the cecum, but no peritonitis exists, and it is no more likely to arise from this cause than from ordinary constipation, which often causes pain and rise of temperature. Correctly speaking, then, peritonitis localized in the immediate neighborhood of the cecum

and characterized by the well-known symptoms may, with the rare exceptions referred to, be attributed to an inflammation of the vermiform appendix in some one of its numerous stages. This inflammation may be a comparatively mild catarrhal one, affecting little more than the mucous membrane, or it may have rapidly passed through various stages to complete gangrene of the organ. I must therefore prefer to use the term inflammation of the appendix, or appendicitis, and give up, once and for all, the terms perityphlitis, paratyphlitis, extraperitoneal abscess, etc., as misleading and not valuable except in explanation of secondary (p. 677) pathological processes. In regard to the so-called extraperitoneal abscess as a result of inflammation of the appendix, there remains nothing to be said to any one who has read Dr. Wier's admirable paper in the "Medical News" for April 27th of this year. The statements and observations which Dr. Wier there makes are perfectly convincing, and I have often confirmed many of them during an operation. As a late result of a much-neglected case, pus may force its way through the lateral or posterior peritoneal lining of the abdomen, but even in very old cases this must be a rare condition, and I have myself never met with such a one. All of these abscesses originating in inflammation of the appendix are intraperitoneal. Inflammatory adhesions, which glue together the adjacent coils of intestine, prevent the contents of the abscess from flowing into the pelvis or among the intestinal folds. At every point the pus is bounded by peritoneum. All of the operations done by the Willard Parker method require section of the peritoneum which forms the anterior wall of the abscess. I have dwelt upon this point because it is a very important one, and one's views in regard to it will determine his operative methods. In this connection I must refer to two other terms—extraperitoneal abscess and extraperitoneal incision for the opening of such abscesses. These again are very misleading, and imply that uninflamed peritoneum can be pushed away from the iliac fossa, the connective tissue broken through, and the abscess evacuated. If these abscesses are, as I have stated, *all* (with possibly a very rare exception) intraperitoneal, then, of course, these terms are false

and misleading. The peritoneum may be pushed back and the abscess incised deep in the iliac fossa by a roundabout and unsurgical method, but when incised the peritoneum will be cut. In the present state of surgical opinion, it remains with those who claim that they meet with extraperitoneal abscesses and make extraperitoneal explorations to prove their point. In not a single one of the early operations for appendicitis which I have done and seen done has there been the slightest doubt as to the fact that the incipient abscess was entirely within the peritoneal cavity. I mean that this fact has always been demonstrable to the satisfaction of every one present. This one must consider as a valuable piece of evidence, for the observations were made at a period in the disease when there could be no obscurity as to the actual condition present. Weir has clearly shown also, in the paper already referred to, by carefully analyzing the reports of one hundred autopsies, that in no one of them did the abscess originate in the extraperitoneal tissue, and that in only four was pus found there at all. Weir also states, when referring to the difficulty of demonstrating the intraperitoneal origin of these abscesses after a considerable abscess has formed, that in only eight out of twenty-six abscesses opened by him could he "recognize that the inner wall of the abscess was made up of loops of intestine bound together by adhesions." But, as I have already said, *no difficulty* is found in making this demonstration when an operation is done at an early stage of the disease.

In these early operations I have found a very varied condition of the appendix and its surroundings, from a mild catarrhal condition of the mucous membrane accompanied by some infiltration and thickening of the submucous and other tissues, to the state of complete gangrene of the whole organ, with more or less extensive peritonitis.

In one instance I removed the appendix from a young lady who in the course of little over a year had had no less than twelve attacks of so-called perityphlitis. These attacks had been severe, giving rise to great pain with rise of temperature, and causing alarm not only to the members of her family, but to her medical attendants, two of these at least being as careful observers as

exist in New York. The operation was done during a period of complete health and after careful consultation, to prevent recurrence. The appendix was found rigid and swollen, the mucous membrane mildly inflamed, the other tissues of its walls greatly thickened. Not the slightest evidence of peritoneal inflammation or adhesion existed. The appendix was readily removed and the patient made a rapid recovery. The operation was done nine months ago. Since that time the patient has enjoyed unbroken health, has resumed active exercise, and has gained twenty pounds in weight. In another case, also a young lady, attacks of abdominal pain, accompanied by vomiting, exquisite tenderness in the right iliac fossa, and considerable elevations of temperature, had occurred on four different occasions. This patient had also been taken care of by the most competent men. Curiously enough, just at the time of this patient's last attack her sister died without operation from a violent purulent peritonitis caused by perforation of the appendix. Subsequently to this last attack and during a period of complete health I removed the appendix after careful consultation with her physician, Dr. J. W. McLane, to prevent recurrence. A condition of disease somewhat in advance of the case already narrated existed. The appendix was quite firmly bound by old adhesions to the under surface of the intestinal mesentery and to the cecum. The mesentery of the appendix had been nearly obliterated; the organ itself was dark-colored, considerably swollen, but soft. The mucous membrane was very dark-colored and swollen, and inclosed some fine fecal grains. Two partial strictures of caliber existed which produced retention of a dirty brown fluid. The evidences of former limited peritonitis existed on the neighboring portion of the cecum. This patient also made a rapid recovery, being out of bed at the end of two weeks, with a wound completely healed. The operation was done over four months ago, and the patient had remained in perfect health, having gained largely in weight and having resumed active exercise from which she had been entirely debarred. These two cases are quoted at this point to show that comparatively slight conditions of inflammatory disease in the appendix may give rise to threatening

illness, which by some would be described as resolving perityphlitis without further explanation. There can be little doubt that both of these cases were preparing for abscess or general peritonitis.

In other cases—all in an acute stage of inflammation—and which will be quoted later, the conditions found have been these: In one the appendix formed a considerable cyst containing nearly an ounce of dark-brown pus. No communication with the cecum existed.

(p. 678) In several the appendix was swollen, discolored, diseased throughout, but gangrenous only at one or two points where perforation had occurred, and in these cases one or more fecal concretions existed, either within or just outside of the appendix.

In several the appendix was in general only moderately diseased, but perforation had occurred, and quite firm recent adhesions had tied the appendix to some adjacent part, doubling it upon itself and so inclosing a small collection of pus with or without concretion.

In two cases the appendix was thick, but flattened so as to be with difficulty recognized, and very firmly bound to the under side of the cecum, and in two cases the appendix was completely gangrenous. In all of these acute cases peritonitis existed—usually a plastic peritonitis of greater or less extent—always involving the cecum and generally the adjacent intestinal coils and abdominal walls. In one case the omentum was quite extensively involved, partly enveloping the appendix. In *no* case was the appendix more than lightly attached by adhesion to the peritoneum covering the iliac muscles, and in none was *extraperitoneal* inflammation observed, excepting sometimes in the anterior abdominal wall. In most cases some pus was found more or less confined by adhesions within a limited area, and in one absolutely no adhesion of any kind existed, though the appendix was perforated by concretion, and very foul pus filled the pelvis and ran freely upward beside the colon.

The pathological conditions of the appendix, as compared with the symptoms in my own cases, most positively show that

one can not with accuracy determine from the symptoms the extent and severity of the disease. I therefore doubt the safety of the advice given by several recent writers, to watch the symptoms and to be guided by their violence in determining the method of treatment. This will appear more clearly in the histories of the cases. I should like now to refer to some of the special symptoms *the weight and value of which have been subsequently determined by an immediate operation*, for it is in this manner that we shall mostly advance our knowledge of the pathology of appendicitis. By autopsy we can not learn very much more in this direction if one may judge by the length of time it required to learn the important single fact that abscesses originating in the appendix are almost invariably intraperitoneal. Pain to a greater or less extent is present in all cases of appendicitis, but many a mistake has been made and a golden opportunity lost by looking for pain in the iliac fossa and an *absence* of pain in other parts of the abdomen. General abdominal pain is often all that the patient will complain of in the first few hours of his attack, and in many cases it requires a careful and pointed examination to determine that the cause of the pain is situated in the iliac fossa. But after the first few hours it becomes more and more evident that the chief seat of pain is at that point, and the general pain then usually subsides. The epigastric region is frequently the point first complained of. One patient, who died on the third day from violent septic peritonitis from perforation, complained of comparatively little pain even when the iliac fossa was firmly compressed. The *exact* locality of the greatest sensitiveness to pressure has seemed to me to be usually one of importance. Whatever may be the position of the healthy appendix as found in the dead-house—and I am well aware that its position when uninfamed varies greatly—I have found in all of my operations that it lay, whether thickened, shortened, or adherent, very close to its point of attachment to the cecum. This, of course, must, in early stages of the disease, determine the seat of greatest pain *on pressure*. And I believe that in every case the seat of greatest pain, *determined by the pressure of one finger*, has been very exactly between an inch and a half

and two inches from the anterior spinous process of the ilium on a straight line drawn from that process to the umbilicus. This may appear to be an affectation of accuracy, but, so far as my experience goes, the observation is correct.*

Chill and vomiting are frequent, but so often absent as to be in no sense of much diagnostic value. Fever to some extent is present in all cases, but very different in degree, some severe cases having a temperature on the first day of less than 100.5° , others rapidly reaching a temperature of 103.5° . But, as nearly excluding non-inflammatory pains, the presence of this symptom is certainly of importance. Rigidity in the abdominal muscles, generally much more marked on the affected side than on the other, I have found very constant, and I believe it to be a sign of value.

Abdominal distension by tympanites varies greatly, and its degree by no means measures the severity of the diseased process. It may be very decided during the very first hours of a mild case, and also entirely absent in the worst form of sudden perforation. It must, of course, be influenced greatly by the condition of the patient's bowels, the ease with which the intestine in each individual is brought to a state of paresis, and by many other causes. But when the gut has been found during the operation to be overdistended, the portion of gut so affected has always been the large intestine. Probably pareses from the local peritonitis is here a large factor.

Tumor of greater or less size I have usually been able to detect at a very early stage, but the composition of this tumor, as shown during operation, has varied greatly. In one case the tumor consisted of the distended unruptured appendix, which was partly wrapped in an inflamed and thickened omentum. In another it was formed of a mass of intestinal coils swollen and glued together by recent plastic exudation. This tumor was large, quite firm, and gave one the impression that a large quantity of pus was present; but only a very minute abscess was

* Since reading this paper I have carefully observed three other cases. In two the point of pain shown by pressure with one finger was two inches, and in the other an inch and seven-eighths from the anterior spine.

found, and that was situated quite beneath the cecum. But under ether some tumor can invariably be detected; and this agent will, I think, be found to be a valuable help to diagnosis in some doubtful cases. The tumor may be dull on percussion, as when pus has formed and lies against the anterior abdominal wall; but I have more than once found a small deep tumor containing pus, which was so completely (p. 679) covered in front by intestines that the percussion note, before ether was given, was purely tympanitic. The pulse during the onset of appendicitis is usually rapid and irritable. The patient prefers to have the right thigh elevated, and objects to its overextension. Rectal examination at the onset I have not found of any value.

The combination of symptoms present will usually render a correct diagnosis as to the seat of the disease quite easy, but in reference to the stage which the disease has reached—that is, whether pus has formed or not, whether the appendix is already perforated or not, even sometimes whether already general septic peritonitis exists or not—the diagnosis is often very doubtful. I remember one case where Dr. Sands performed a beautiful operation and saved the patient's life. At the consultation held before operation four gentlemen were present. Three of them had certainly seen many cases of appendicitis. Three quite different opinions were expressed. Dr. Sands thought that the appendix was perforated, and that pus had formed. One of the others thought that there was probably appendicitis, but advised an extraperitoneal incision. Another thought the case so mild that it should be treated without operation. Dr. Sands operated by an incision along the right edge of the rectus muscle, opened an intraperitoneal abscess just in the middle of his incision, and removed a perforated and sloughing appendix. The patient rapidly recovered. This case occurred very shortly after Dr. Sands read his last paper before this society. I mention it to show that the diagnosis of the exact condition in such cases is not easy. A means of diagnosis lauded by some, permitted by others, and totally condemned by a few, is the exploring needle. I believe that the use of this instrument will become less and less frequent as we know more of the disease. While perhaps

occasionally permissible at a late stage of the disease, it is certainly to be condemned at its beginning. The discovery of pus with the syringe is, to be sure, gratifying to a hesitating operator, but the withdrawal of an infected needle through several layers of peritoneum, which it may have passed during its introduction, can totally nullify a good subsequent operation. And, if the needle does *not* discover pus, which has often happened even when that fluid has been present in considerable quantity, then the man who pinned his faith on a needle is induced to underestimate the importance of the case and its mode of treatment.

Some years ago I went a long distance into the country prepared to operate upon a nine-days-old abscess, the result of appendicitis. There existed a large fluctuating tumor, and the case was plain and needed just one cut. But the family physician was very conservative, and said the time had not come, and that there was no pus. I was in despair, for the journey took many hours. Fortunately, I had a good hypodermic syringe with me. The doctor said rather superciliously that that thing was harmless anywhere. So he permitted its introduction; and when the barrel filled with pus he yielded to an operation, and treated me afterward with great respect. But to search for pus with a needle, first in one direction and then in another, at the risk of doing harm, and with no certainty of acquiring any real information, is a practice as unsurgical as it is unnecessary.

I think that there is still much misapprehension in the minds of many practitioners as to the symptoms produced by perforation of the appendix. Many associate with this condition, and with no other, a very violent onset of the disease with quite well-marked symptoms, as compared with the less severe commencement of a slowly forming abscess. The truth is that, in the early stage, no accurate diagnosis can be made as to whether the appendix is perforated or not, excepting in those cases where comparatively mild symptoms *suddenly* become much aggravated, when perforation or the rupture of an abscess may be inferred. Perforation often occurs with but few symptoms at the very beginning of the disease, but, being preceded by the formation of more or less plastic adhesion of the appendix, no sudden in-

crease in the severity of the disease occurs at all. An abscess slowly forms, which may increase to a considerable size without being discovered, and then force its way, or proceed by infection, in the most dangerous directions. The comment might fairly be made upon this description of the early symptoms of appendicitis that the diagnosis of the disease is very obscure and uncertain. To the careful observer it is not difficult, however, to determine as to the existence of the disease. The only real difficulty lies in determining within the first few hours what the future progress of the disease is to be in deciding whether firm adhesions are forming, which will effectually exclude pus from the general peritoneal cavity, and so provide for subsequent safe evacuation of abscess, or whether no such protecting wall exists, and an overdilated appendix threatens to instantly set up a fatal peritonitis. If this difficulty could be set aside by a more careful study of symptoms, and without losing valuable time, our course would be clear, and we should no longer helplessly hesitate as to when to operate and when to stand aside. There is no reason to think, however, that diagnosis from symptoms alone will ever reach that perfection. We need some further aid to diagnosis; some positive and rapid means of determining what method of treatment we are to adopt. We have reached a point where we can never be satisfied with the mortality that attends an expectant treatment. What we wish to accomplish in the treatment of appendicitis is, not to save half of our cases, nor four cases out of five, but *all of them*; and how is this end to be attained except by improved methods of diagnosis at the very earliest stage of the disease? I hope that I may never again go every day to visit a threatening case, waiting bashfully for the authority of a clearly defined general peritonitis before I dare take action. I do not mean to deny that many very ugly-looking cases of appendicitis go on to the formation of abscess which may be safely opened and end in complete recovery; we have all of us seen many such. I am well aware that numerous cases have presented all the symptoms of the disease, have become very ill, and have finally recovered without any operation. Within two years I have seen two cases, in one of which the patient was

so ill that I refused to operate, and in the other case I strongly urged operation and was refused permission. Both of these patients recovered after long illness without (p. 680) operation of any kind. Probably the abscesses emptied themselves at some point into the intestine. But such unexpected recoveries, and the frequent formation of abscesses which can be opened safely at a later stage, even the many cases which quite rapidly terminate, at least temporarily, without suppuration, do not console us for the heavy mortality caused by appendicitis. What this mortality has been we shall of course never know. We do know that the cases which are recognized and which die are numerous, and it is safe to assert that a very large number of fatal cases of peritonitis commence with an unrecognized inflammation of the vermiform appendix. No one will dispute that if we could so improve our methods of diagnosis that we could recognize within the first few hours the serious nature of many cases, we would operate in these cases at once, willingly preferring to incur the risks of an operation rather than face the certainty of death that septic peritonitis implies. How may we improve our methods of diagnosis? At present I see no clearer road than the exploratory incision permitting a direct inspection of the parts and a complete study of the disease. If it can be shown by future experience with improved methods of operation, and with more perfect antiseptic precautions, that the exploratory incision for the inspection of the diseased appendix is much more free from danger than the expectant treatment, then there could be but one answer to the question, What is the best treatment? The firm conviction that very early operation for the cure of appendicitis can, with proper care, be done with very slight risk, has induced me to subject a considerable number of these cases to the earliest operation possible, and my chief purpose to-night is to present to you the results of my work in this direction. It is proper to state that no case of appendicitis has been refused operation, and that all the cases operated upon in the early state of the disease are here reported:

Case I.—E. M. P., a young gentleman nineteen years of age, complained of general abdominal pain at 11 A.M. on May 21, 1888. The

pain was regarded as due to indigestion, and was treated with family remedies. In the afternoon the patient fainted, and by four o'clock his pain had greatly increased in severity. He received a little morphine and hot applications were applied. At 5 P.M. his mouth temperature was 98.4° , his pulse 100. During the night and the following day the patient complained sometimes of severe pain, and occasionally felt much better; he took a considerable quantity of milk, and at 8 P.M. his temperature was only 100° . During the second night he suffered much pain, and at 5 A.M. on the 23d it was noted that his pain was chiefly in the right iliac fossa. At 5.30 he had a severe chill and his temperature rose to 103° , his pulse to 120. At this time he was visited by his physicians, Dr. Fessenden N. Otis and Dr. William K. Otis, who diagnosticated at once acute appendicitis, and requested me to see the patient. This I did at about 8.30. I found the pulse and temperature as stated, and the following condition: Great rigidity of right abdominal muscles; exquisite tenderness on pressure at a point just two inches internal to the anterior spine of the ilium, in the direction of the umbilicus. Beneath the finger at this point could be felt a small resisting mass, less than one inch in diameter. No dullness on percussion anywhere. General appearance excellent. The diagnosis of appendicitis already made by Dr. Otis was confirmed by myself, and an hour later by Dr. Sands. Immediate operation advised and accepted.

General appearance of patient excellent. It should be noted that at 11.30 the temperature had fallen to 101° .

Operation at 12 o'clock, just forty-nine hours from the first pain. Present, Dr. F. N. Otis, Dr. William K. Otis, Dr. L. R. Morris, and Dr. Tuttle.

Ether anesthesia. A slightly oblique incision four inches and a half long, the center of this incision being two inches from the anterior iliac spine toward the umbilicus. Tissues of abdominal wall quite markedly edematous, particularly near the peritoneum. On opening the peritoneum freely, the appendix came at once into view. It was larger than a man's thumb, dark-brown in color, tense, evidently full of fluid, and at no point gangrenous, but its wall evidently nearly as thin as paper. A tail of omentum partly enveloped it, and this was much inflamed and freshly adherent. Everywhere else the peritoneum was healthy, and not an indication of the formation of any bounding wall of adhesions existed. Coils of small intestine surrounded this full-to-bursting sac. The omentum was gently separated and the inflamed portion ligated and cut away. The mesentery of the appendix was carefully tied in

sections, and the base of the appendix dislodged from an inverted pouch of cecum, ligated at its base, and cut away. It proved to contain at least half an ounce of very foul brown pus, but no concretion. Its communication with the cecum was closed by stricture, so that the unbroken, purulent, acutely inflamed cyst was removed entire. The stump was disinfected with a 1-to-1000 bichloride solution. Two silver-wire sutures passing through the whole thickness of the abdominal walls closed the upper part of the wound, and one similar suture the lower part. The central portion was loosely packed with iodoform gauze down to the ligated stump. Dressing of iodoform and bichloride gauze over all.

At 6.40 P.M., less than six hours after the operation, patient's temperature was 99.8° and pulse 80. A small quantity of morphine was given for wound pain. The dressings were changed on the third day, and a perfectly aseptic condition of wound found. This patient made a rapid and absolutely unbroken recovery, and is today perfectly well.

This is, I believe, the first recorded case where an acutely inflamed unruptured appendix has been removed full of pus. Who can doubt what the result would have been in this particular case had the cyst ruptured, and the operation been delayed a few hours? Would not the opportunity for recovery have been lost had the advice so often and so recently given been followed—to delay operation until symptoms of spreading peritonitis appeared?

Case II.—John S., ten years of age, was admitted to my care at the Roosevelt Hospital on August 19, 1889. He gave no history of previous attacks. A week ago he became ill, and complained of general abdominal pain. He went to bed, and says that since that time he has been feverish and has not been free from pain. Four days ago the chief seat of pain is said to have been in the right side and low down. On admission his pulse was 110, his temperature 103.4°, and he was nauseated. Between the umbilicus and the right iliac spine was noted a considerable tumor, which was markedly tender on pressure. The percussion note over the tumor was dull. No tympanites existed. The general appearance of the patient was that of severe illness. I operated on the same day. The usual incision was made, and the tissues found in a normal condition down to the peritoneum. The anterior peri-

toneum itself was perfectly uninflamed, and uninflamed small intestine covered the anterior face of the tumor. When these were drawn toward the median (p. 681) line, a mass of adherent intestines were disclosed, which inclosed a small indurated tumor.

The intestinal coils were gently separated on the anterior face of the tumor, and several drachms of fecal pus at once escaped, emptying a cavity somewhat tubular in shape and large enough to admit the finger. The appendix lay in this cavity, congested, much swollen, and infiltrated with pus. No perforation existed, and no concretions were found. The appendix was tied off with silk and removed. A rubber drain was introduced, the cavity packed with iodoform gauze beside the drain, and a full antiseptic dressing applied.

On the following day, August 20th, the boy's temperature was 99.6° as against 103.4° the day before, a reduction in less than twenty-four hours of nearly four degrees. This patient recovered rapidly and completely, and on September 25th his wound was entirely healed.

Case III.—W. K., a male, sixteen years of age, was admitted to my care at the Roosevelt Hospital on July 26, 1889. Previous history negative. Forty-eight hours before admission first felt pain in the right iliac fossa. On the next day diarrhea set in; abdominal pain was quite general, though more distinctly localized in the right iliac fossa than elsewhere, and this increased up to the time of admission to the hospital. The patient's temperature was then 102° , his pulse 110. The abdomen was slightly distended and tympanitic. In the right iliac fossa was found a small, very tender non-fluctuating tumor, which lay just inside of the anterior iliac spine. Diagnosis, acute appendicitis.

Operation at 3.30, July 26th. The usual incision was made. Beneath the incision were found normal non-inflamed intestines. These were drawn toward the median line, when the appendix was found projecting stiffly forward and slightly upward by the inner side of the caput coli.

It curled around the end of the cecum and then turned upward and forward. Slight recent adhesions tied the appendix at its base only to the cecum. At other points it floated freely among non-inflamed intestines. The adhesions were broken down and the appendix ligated at its base and removed. It was six inches and a quarter long, edematous, and much thickened and inflamed throughout. Minute foci of

pus were scattered through its substance, but there was no concretion and no perforation. On its removal the seat of operation was left perfectly clean, but, to insure safety, a rubber drain was passed through the loin directly to the base of the stump, and the anterior wound was partly closed and partly packed with iodoform gauze. The next day patient's temperature was 100°. His wound was inspected, but not dressed completely until July 30th. No pus was found. The patient made an unbroken recovery without incident, and his wounds were completely healed on August 19th.

Case IV.—Annie O., eighteen years of age, was admitted to the medical wards of the Roosevelt Hospital on May 29, 1888. Six years ago she had an attack similar to the present one from which she entirely recovered without operation. Two days ago she was seized with severe epigastric pain accompanied by fever and headache, and tenderness on pressure in the right iliac fossa. On admission, the abdomen was tense, tympanitic, tender on pressure at all points, but more especially in the right iliac fossa. Here a small tumor is distinctly felt. I saw this patient for the first time on May 30th, and, having expressed the opinion that she should be operated upon at once, she was transferred to my care. At this time her symptoms had become much more threatening; abdominal distension was extreme. Her temperature was low, 100.4°, pulse 100, respiration 36. I operated at once, making the usual incision. The tissues of the abdominal wall were edematous and the deeper ones much fused together. Beneath the center of the incision the distal end of the appendix was readily found. It was much enlarged and thickened, and greatly discolored. At first no pus was seen, but, on gently separating the end of the appendix from adjacent parts, a small cavity was found beneath it containing less than one ounce of pus. The cavity was cleaned with hot water, and it was then seen that the appendix was perforated at about its middle and lying in the perforation was a large fecal concretion. The whole appendix was then removed after ligating the base, the cavity was swabbed out with 1-to-1,000 bichloride solution, two rubber drains introduced, and the cavity packed with iodoform gauze. A complete antiseptic dressing was applied. On June 1st the patient's temperature was 99°, pulse 100, respiration 18. Abdomen free from pain or distension.

This patient made an unbroken recovery, being out of bed on June 23rd, with a small, superficial, flat ulcer still to heal.

Case V.—Charles E. A., twenty-five years of age, was admitted to the Roosevelt Hospital on September 1, 1889. Patient gives a history of probable appendicitis occurring five months ago.

Two days ago, after several weeks of abdominal discomfort, the patient was seized with severe abdominal pain, nausea, vomiting, and fever.

On admission, his temperature was 102°. Internal to the anterior iliac spine, on the right side, some resistance and tenderness on pressure were noted. Diagnosis, appendicitis.

On September 2d, under ether narcosis, the usual incision was made, the tissues of the abdominal wall being found very edematous. Marked adhesions and thickening of the peritoneum were found over a large area, indicating clearly the existence at some previous time of a quite extensive peritonitis. This probably occurred during the attack referred to above. The appendix was found, after some difficulty, hanging over the edge of the pelvis, greatly thickened and hardened. After being freed from adhesions, it was ligated close to its base and removed. The immediate neighborhood of the stump was cleansed and the space packed with iodoform gauze. The upper portion of the abdominal wound was closed by suture. With the exception that a slight superficial abscess developed beneath the suture line, this patient made an easy recovery, and was discharged, with a wound completely healed, on October 17th. This patient was operated upon by Dr. Frank Hartley, my first assistant at the hospital.

Case VI.—Miss E. C., twenty-five years of age, a patient of Dr. W. T. Alexander, of this city, had complained of a sense of uneasiness and discomfort in the right abdominal region, low down, for two or three weeks. She had, however, gone about as usual, and walked several miles daily. On June 18, 1889, in the evening, she was seized with severe general abdominal pain, most severe in the epigastrium, and was nauseated. She went to bed, and was then first seen by Dr. Alexander, who diagnosticated appendicitis, and ordered hot applications and a little morphine, with complete rest in bed. On the following day Dr. Alexander asked me to visit the patient. This I did in the afternoon. The patient's temperature was then 101°, and her pulse 100. She had a very ill look, and complained bitterly of the slightest pressure over the right iliac fossa and of some tenderness all over the abdomen. I advised immediate operation. There were present at the operation

Dr. W. T. Alexander, Dr. G. T. Jackson, and Dr. R. P. O'Neill, and these gentlemen assisted me.

I made the usual incision. The tissues of the abdominal wall were normal, and within the peritoneal cavity scarcely the slightest trace of adhesions was found. The appendix, nearly completely gangrenous, as large as one's middle finger, lay just outside of the caput coli, not perforated, but containing two large fecal concretions, just ready to escape through very soft (p. 682) gangrenous tissue. A little purulent fibrin lay beneath the appendix. No limiting wall of any kind existed, and reddened small intestine lay above and below. The mesentery of the appendix was carefully and with some difficulty tied off, the appendix ligated at its base and removed. The immediate neighborhood was then thoroughly cleansed with 1-to-1,000 bichloride solution, dusted with iodoform, and packed with gauze. A rubber drainage tube was introduced beside the gauze down to the stump. The upper part of the incision was closed with two sutures. The patient suffered from nausea and tympanites for two or three days, when her temperature fell to normal and remained so. On the seventh day the wound discharges were decidedly fecal, and continued to have this character for about a week. The wound then became perfectly healthy and rapidly healed. This patient has gained greatly in health and weight, and has been, up to date, perfectly well.

Case VII.—Edgar C. B., a stalwart young man, twenty-one years old, complained of pain in the lower part of the abdomen during the evening of January 13, 1889. The next morning, when he had gone to work, this pain spread through the whole abdominal cavity and became very severe. He reached home with difficulty and went to bed. During the afternoon of the 14th—that is, at the end of about twenty-four hours—the pain localized itself chiefly in the right iliac and lumbar regions. At noon on the 15th he had a chill, and, feeling very ill, came to the Roosevelt Hospital in the evening. His temperature was then 101.6°, pulse and respiration about normal. The abdominal muscles on the right abdominal half were rigid, and very acute tenderness was complained of when pressure was made over the right iliac fossa about two inches inside of the anterior iliac spine. No tumor could be felt. The diagnosis of acute appendicitis was made, and I determined on an immediate operation. This was done at 11 P.M., as nearly as possible forty-eight hours after the first symptom. The usual incision was made. The tissues of abdominal wall were found in a normal condition. Be-

neath the line of incision were coils of non-inflamed small intestine. These were pushed inward, exposing a mass of small intestines matted together by adhesions and quite free from the iliac fascia. After a short search, and after breaking down some of these adhesions, the appendix was found, passing backward and inward from the cecum, then doubling back upon itself. It was closely tied by adhesion to the cecum and adjacent mesentery. The adhesions were broken down, the mesentery of the appendix tied off in sections, and the appendix itself ligated at its base with catgut and removed. The appendix was much diseased, thickened, and distorted, but not ruptured. On section I found within it some black, semi-fluid material. The mucous membrane was gangrenous throughout, and the wall of the appendix at one point gangrenous as far as the peritoneal coat. The stump was sponged with 1-to-1,000 bichloride solution. The upper part of the wound was closed with silver stitches, a rubber drainage-tube passed down to the stump, and the open wound packed with iodoform gauze. During the next twenty-four hours considerable pain was experienced, and for a few days constipation was obstinate. On the morning of the 17th, the temperature became normal and remained so throughout convalescence, which was unbroken and entirely completed by February 11th. A small superficial ulcer was completely healed on February 21st.

Case VIII.—C. G. McK., a young gentleman twenty-three years old. First attack of pain in right iliac fossa two years ago. Second attack in May last, when he was confined to bed five days with fever and severe pain and tenderness in the same region. On Thursday morning, October 17th, he had a sudden attack of severe pain in region of appendix, went to bed, and his temperature was noted to be 99°. In the evening his temperature rose to 100°. Pain and tenderness steadily increased. Friday he remained in the same condition, and was seen by me, at the request of Dr. E. E. Swift, later at night. The patient was haggard and looked ill. Tenderness on pressure about two inches inside of the iliac spine was very marked. An ill-defined tumor existed, and decided distension of the abdomen. Operation was advised, but the circumstances were such that it was postponed until twelve o'clock on the following day.

Operation October 19, 1889. Ether anesthesia. The usual incision was made. On opening the peritoneum, an enormously distended caput coli filled the wound and rendered the search for the appendix extremely difficult, forcing me to handle the intestines far more than was to be

desired. The appendix was at last found, flat, wide, and so firmly adherent to the under surface of the cecum as to be identified with great difficulty, and numerous firm old adhesions prevented the free movement of intestines and at one point formed a nearly constricting band. An indurated mass beneath the center of the appendix was opened with the finger by separating adhesions which, however, were very strong, and many of them evidently old. From this mass about a drachm of foul fecal pus escaped and was sponged away. The difficulty of dissecting away the appendix was so great that I was finally obliged to desist and to be satisfied with removing only that portion of it which formed the wall of the abscess. The cavity was very thoroughly cleansed, and an attempt made to return the prolapsed large intestine and close the wound. This was found to be exceedingly difficult, owing to the very excessive distension of the gut, and much time was expended and much handling of gut necessitated. Finally the wound was closed as in other cases, the lower part being packed and drained. The patient recovered well from the effects of the operation, but at the end of twenty-four hours his temperature rose to 102° , and the abdominal distension increased. He was bright and looked fairly well, however, and I did not expect serious illness. His temperature, however, continued to rise, symptoms of peritonitis developed, complete paresis of bowel persisted, and the patient died at the end of four days, of peritonitis. No autopsy could be obtained.

Whether the difficult and unusual handling of the intestines was the chief cause of peritonitis, or whether constricting bands, formed by old adhesions, caused actual obstruction, I am unable to say. No movement of the bowels could be obtained and no flatus passed after the operation excepting by the aid of a long rectal tube. Certainly the peritonitis was not septic, and such was the opinion of Dr. Delafield and Dr. Swift, who visited the patient with me. Moreover, when, on the second day, I removed the packing, I found a perfectly healthy wound, without the slightest sign of infection. One thing is clear—that, had the operation been done during the patient's first attack two years ago, none of the great difficulties which I met with would have been encountered.

I stated at the beginning of this paper that I did not here intend to review the treatment of appendicitis in a systematic manner,

but I should not do justice to the real subject of this writing were I to drop the matter at this point. I must, in the first place, as accurately as possible, define the class of appendicitis to which I have applied the method of treatment described; and then I wish to devote a few minutes to a description of the technique of the operations. I have presented eight cases of appendicitis operated upon at an early state of *acute* inflammatory process. These eight cases include *all* of those (p. 683) operated upon since May 20, 1888, to date. Previous to May 20, 1888, I had never operated upon a case except by the older methods. During this period of eighteen months I have seen and operated upon a much larger number of cases of appendicitis at late stages in the disease—that is, when extensive abscess has existed, and in some cases of early general septic peritonitis due to appendicitis. Such cases are excluded from the list given, as belonging to an entirely different category. I have measured the stage of the disease, not by the number of hours or even days that it has existed, but by the character and extent of the inflammatory process, all cases being included in the list excepting those where it was clear that large, comparatively safe abscess was forming, or where general septic peritonitis was already established. I should, moreover, state that in every case operation has been done as soon as possible after being seen, excepting that in the fatal case various circumstances, contrary to my wish, necessitated a delay of about twelve hours. In no case has a diagnosis of appendicitis been made which has been subsequently proved by operation to be incorrect. To those who have been in doubt as to whether the operation or the disease carries with it the most danger, I think these cases, although limited in number, must be convincing in favor of the operation. All will acknowledge that every case of appendicitis may, so far as the cleverest observer can tell, have to pass by many very dangerous obstacles before reaching the smooth water of a comfortable abscess. For my part, I would endeavor to insure safety early, before reaching the rapids, rather than trust to finding my way with my eyes blindfolded through a dangerous passage. I am familiar with the good-natured jest that the surgeon is now ready to cut every

one who has a stomach-ache. The death-rate from appendicitis within the professional circle of New York alone is a sufficient answer to that criticism.

How I should be much misunderstood if I should give the impression that, while I believe the operation to be less dangerous than the disease, I also believe the operation to be simple and easy of execution. I look upon it as often an exceedingly difficult one, and one which requires as much care and patience and attention to detail as any with which I am familiar. Moreover, I have never seen two cases of appendicitis operated upon in which the pathological conditions, the position of adhesions, the relation of surrounding parts, etc., were very nearly alike. Every case presents some new problem, and in every case there is large opportunity for the exercise of careful judgement as to how best to meet this or that difficulty. Of course there must be pioneers, as Sands was, and such may be the most successful, but my strong feeling is that it is well worth while for any one who may have to do this operation to see it done, at least once, first.

Before describing the steps of the operation, I refer again to the important aid to diagnosis of which I have already spoken—namely, the ascertaining, by the pressure of a single finger-tip, that the point of greatest tenderness is, in the average adult, almost exactly two inches from the anterior iliac spine, on a line drawn from this process through the umbilicus. Much greater tenderness at this point than at others, taken in connection with the history of the case and the well-known signs, I look upon as almost pathognomonic of appendicitis. This point indicated the situation of the base of the appendix, where it arises from the cecum, but does not by any means demonstrate, as one might conclude, that the chief point of disease is there. The abscess, or concretion, or cyst may be at quite a little distance, but the greatest pain, on pressure with one finger, will be felt at the point described.

The incision should be a liberal one, for much room may be required, and a five-inch cut in the adult is not too much. It should follow as nearly as possible the right edge of the rectus muscle, and the center of the incision should lie opposite to or

a little below the anterior iliac spine, on a line drawn to the umbilicus. When the external oblique aponeurosis is cut through by this incision, the aponeurotic structure, in which the other abdominal muscles end, comes into view, and is easily divided without cutting muscular fiber. Then the fascia transversalis, the subperitoneal fat, and the peritoneum are cut in succession. If pus has formed close against the anterior abdominal wall, these last-mentioned tissues will be found infiltrated with serum, or even thickened so as to look like cheesy tubercle. Otherwise these parts may appear perfectly normal. On opening the peritoneum the appendix may at once be seen, or adhesions and inflammatory exudations may have so distorted the parts that a careful and difficult search may be required to find the appendix at all. It may be flattened out and glued firmly to the inflamed surface of the cecum by old and recent adhesions, or it may be coiled upon itself and buried out of view in a mass of lymph. The finger is often quicker than the eye to detect the appendix in these conditions, as it is very certain to be found where the greatest thickening, as felt by the finger, exists. More than once I have had to turn the cecum out of the wound and examine carefully the usual region of origin of the appendix before I could identify it. Usually then with the finger or a dull-pointed instrument the adhesions can be broken down or tied off, as may seem required by vascularity. If the appendix has been thus separated, I have usually tied it off with silk or catgut close to the cecum and cut it away, and generally between two ligatures. Careful disinfection of the stump should be made. I have scraped its interior and disinfected with 1-to-1,000 bichloride solution, and then rubbed in iodoform. Once, when it looked dangerous, I tied with silver wire, and then used the fine-pointed cautery to disinfect. If thoroughly cleansed, it seems to be unnecessary to lose time in sewing the peritoneum over the stump, as recommended by Treves. When the appendix has been removed nothing remains to be done but to disinfect the whole neighborhood, insert a drain, and pack the small space with iodoform gauze. The upper half of the wound may perfectly well be tightly closed with stout sutures, which should

include the whole thickness of the abdominal wall—peritoneum as well. In some cases I believe it to be good practice to introduce a large drain by a separate opening well above and behind the iliac spine, for in some cases the region of disease may extend especially in that direction (p. 684). But the question may fairly arise in any case as to whether it is wise to attempt to dissect out the appendix and remove it. If the difficulties of dissection would evidently be very great, I think it is better to open the abscess if there is one, cleanse the cavity, and, leaving the appendix *in situ*, pack and drain the wound.* The packing I have usually removed on the third day and replaced it with less, and the cavity has rapidly granulated. If, at the time of operation, one introduces sutures throughout the whole length of the wound, leaving the central and lower ones loose, these can subsequently, after one or two dressings, be tied, and the wound thus rapidly narrowed. Over the whole wound, of course, a complete dressing is applied, and good bandaging is better than any binder, to prevent the possibility of extrusion of gut by ether vomiting or intestinal distension. None of my patients have developed a hernia at the site of operation. I have kept them all in bed for four weeks or more. None have had any recurrence of inflammatory action of any kind.

A few more words, Mr. President, and I have finished. Are there any contra-indications to this operation in a clear case of appendicitis? I think there are. Very great abdominal distension, which might be in a given case probably be relieved by a few hours treatment, would lead me to delay the operation, for expulsion of intestine is a very serious obstacle to the proper completion of the operation without risk. Unusual obesity I should regard as a good reason for a more expectant method of treatment. But the most important contra-indication of all is the absence of any one of the necessary safeguards and aids, such as the best assistance, the best light, and the best appliances for performing a perfectly aseptic operation.

* In a case operated upon since writing this paper, it would have been a dangerous proceeding to remove the deeply seated and strongly adherent appendix. I broke its wall at one point, and then drained through the loin and packed in front. The treatment was completely successful, and the patient is safely convalescent.

Note.—Since writing the foregoing paper, I have operated in three other cases of acute appendicitis. One of them was that of a lad, fifteen years old, a patient of Dr. G. A. Spaulding's. The operation was done at the fortieth hour of the disease, the temperature being high and the symptoms very threatening. The appendix, much diseased and containing two large concretions, was removed. The temperature fell on the following day to 99°, and has been normal ever since that time. The patient is now safely convalescent.

The second case was that of a patient of Dr. Jarecky's, fifteen years old. The operation was done at the beginning of the fifth day. The appendix, gangrenous at two points as far as the peritoneal coat, was still not perforated even at this late date. It was removed, and the patient is now safely convalescent.

The third patient, already referred to in a note, is nearly well. None others have been operated on in an acute state of inflammation up to date. The number of operations is, therefore, eleven. Of these, one proved fatal, probably from obstruction by a band not discovered.

THE END

McBURNNEY'S INCISION

While professor of clinical surgery at the College of Physicians and Surgeons in New York City, in 1894, at the age of 49, Dr. Charles McBurney proposed a new incision for appendectomy which still bears his name. He then had had charge of the entire surgical service of Roosevelt Hospital for six years, so that his surgical knowledge and judgment must have been founded on at least hundreds of cases. McBurney recommended this new, muscle-splitting or gridiron incision because its use gave a more direct approach to the appendix and reduced the incidence of post-operative incisional hernia. The objections which he listed were (1) a too limited exposure of the abdominal cavity, (2) insufficient room for extensive drainage and (3) the need of two extra assistants to hold retractors. McBurney described a method of enlarging the incision when necessary by continuing the original muscle splitting. He had used the incision in only four cases when he wrote this paper. See following pages for complete article.

Today, 40 years later, the McBurney incision is probably more extensively used for appendectomy than any other. When complete exploration of the abdominal cavity is desired, other incisions (paramedian) are recommended; one of these was originally used by McBurney. Adequate drainage is obtained through this incision by employing rubber tubes or cigarette (gutta-percha and viaform gauze) drains. At the present time the entire abdominal opening is held apart by one pair of retractors, not by four as described by the originator. A further objection that has been given is the liability to right inguinal hernia some time after the operation, caused by injury to the iliohypogastric and ilioinguinal nerves by incision or retractor. The incidence in D. C. Balfour's series (*Railway Surg. Jour.*, 19: 117-119, 1912 and Mayo Clinic Papers, 4: 242-245, 1912) in which, out of 795 patients operated on for right inguinal hernia, 17 had had a previous appendectomy through a McBurney incision, seems small enough to be coincidental. Even these objections can be answered by recommending enlargement of the incision upward rather than downward, minimal injury to tissues by retractors and use of soft, flexible drainage wicks.

The solution to the whole controversy lies in the fact that the McBurney is an efficient incision in properly selected cases and that any surgeon should be prepared to use any known method that will be to the best advantage of his patient.



The Incision Made in the Abdominal Wall in Cases of Appendicitis, with a Description of a New Method of Operating

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SURGEONS are practically unanimous in discarding the median incision of the abdominal wall when operating for appendicitis. The division of the tissues in the median line is very easily accomplished, and the repair of the wound is probably more perfect than when the incision has been made at any other point, but the entrance to the peritoneal cavity, which is thus affected, does not so readily permit the operative work in connection with the appendix within the cavity, or the subsequent treatment of the wound in any case where complete closure of the incision is contraindicated.

The usual situation of the appendix, well to the right of the edge of the rectus muscle, and the fact that abscesses and other lesions arising in disease of the appendix are largely confined to the right half of the abdomen, have led operators, almost without exception, to make their entering incisions either at the

outer edge of the rectus or at some point between this muscle and the anterior spine of the ilium.

In my earlier operations for the removal of the appendix at the beginning of the disease, and in recurrent cases operated upon in the interval between attacks, I always made the incision parallel with and near the right edge of the rectus. The advantages of this incision are that the deeper tissues divided are purely tendinous, that the hemorrhage is slight, and that the suture of the wound, when closure is permitted, is very easy and satisfactory (p. 39). The disadvantage is that the situation of the appendix is usually still farther to the right; indeed, it is often close to the outer part of Poupart's ligament, and, frequently enough, the appendix points upward to the outer side of the colon. In all such cases, if an incision by the side of the rectus is made, the operator is forced to work beneath the overhanging shelf formed by the outer part of the abdominal wall, and the subsequent removal and reintroduction of gauze drainage material, in cases where complete closure is contraindicated, is decidedly interfered with. It has seemed to me that in all cases where it is desirable first to locate the base of the appendix, and usually too where one wishes to make an entrance into an abscess originating in disease of this organ, it is much better to incise the abdominal wall a little to the outer side of the normal situation of the appendix. The inner edge of this wound is drawn inward by a retraction, and but little tissue has to be drawn outward in order to fully expose the caput coli and allow of easy identification of the base of the appendix. Through this incision also, or through a parallel one made still nearer to the anterior spine of the ilium, it is easy to enter, empty, and subsequently treat almost every case of abscess. Of late years I have made almost all incisions for appendicitis about as follows: The incision in the skin is an oblique one about four inches long. It crosses a line drawn from the anterior iliac spine to the umbilicus nearly at right angles about one inch from the iliac spine, and is so situated that its upper third lies above that line.

The incision of the aponeurosis of the external oblique is a little shorter, and practically merely separates the fibers of that

muscle and its tendon without cutting them. The section of the internal oblique and transversalis muscles follows, cutting the muscular fibers nearly at right angles to their course, and is completed only at the central half at first. This deeper incision can be readily lengthened if, after cutting the fascia transversalis and peritoneum, the character of the lesion seems to call for more space. The above description corresponds accurately to the incisions I have made during the last few years in the large majority of cases, although, of course, abscesses unusually placed (p. 40) have required sometimes a larger opening, and sometimes an incision beginning at a higher or at a lower point, or placed much nearer Poupart's ligament. In all of these sections the damage done to the abdominal wall is considerable, and we have all of us been disappointed, especially after operating upon suppurating cases, when it has been necessary to treat abscess cavities with gauze drainage, to find that even very perfect treating of the wound has been followed by small or large ventral herniae.

It can certainly be affirmed that the formation of a hernia subsequent to these operations is not due to any particular *length* of incision, nor can a specially restricted incision insure against the same result.

In regard to the exact length of the incision, I would say that it should be adjusted to the necessities of the case, just as incisions in other parts of the body, made for various purposes, should be adjusted. Incisions should be long enough to allow complete and safe work to be done, and it is most unscientific and harmful to encourage those of limited experience to believe that a special measure of good goes with a special length of incision. If the parts severed in the making of a wound are properly adjusted, and the wound properly treated, repair will be just as rapid and complete whether the wound be five inches long or three inches long, while, on the other hand, no good surgeon will ever unnecessarily divide tissue simply because he can again obtain repair.

When hernia occurs after an operation for appendicitis, it is due to the imperfect repair following the complete section of

a number of superimposed tissues, and it has sometimes followed, both in cases where the incision was made just at the linea semilunaris, and also when made through the muscular wall outside of this line. In abscess cases where a free incision and also open treatment of the wound for drainage are essential to safety, hernia of greater or less dimensions is not unfrequently seen without a year after operation.

By the term hernia, used in this connection, is meant the partial eversion of the cicatrical tissue caused by intra-abdominal pressure at one or more points in the line of the wound, where (p. 41) repair of the deeper tissues incised has been imperfect. Even after operations for the removal of the appendix in the interval between attacks, and when the wound may be completely or nearly completely closed at once, small herniae, of the same variety, are not unknown. The recurrence of hernia is due, first, to the more or less constant intra-abdominal pressure, and secondarily, to the difficulty in obtaining perfect repair in the parts divided. The peritoneum is often very perfectly sutured, the transversalis fascia usually very imperfectly. The external oblique aponeurosis is usually, when its suture is permissible at all, very completely repaired. The greatest defect in repair is due to the section at right angles either of the muscular fibers of the internal oblique and transversalis, or of the tendinous fibers forming the conjoined tendon of these muscles at the edge of the rectus. In either case, the retraction of these muscular fibers, aided by intra-abdominal pressure, tends constantly to separate the edge of the deeper part of the wound, thus permitting at first slight, afterwards increasing, eversion of the peritoneum, and the formation of an incomplete hernial pouch. Such cases require the use of an abdominal belt or other apparatus to give sufficient support to the belly wall. The consideration of this defective result in some cases has led me to attempt a different method of entering the cavity in operations for the removal of the appendix in non-suppurative cases.

The skin incision should be made as already described. The section of the external oblique muscle and aponeurosis should correspond, great care being taken to separate these tissues in

the same line, *not cutting any fibers across*. This is easily accomplished.

When the edges of the wound in the external oblique are now strongly pulled apart with retractors, a considerable expanse of the internal oblique muscle is seen, the fibers of which cross somewhat obliquely the opening formed by these retractors. With a blunt instrument, such as the handle of a knife or closed scissors, the fibers of the internal oblique and transversalis muscles can now be *separated*, without cutting more than an occasional fiber, in a line parallel with their course,—that is, nearly (p. 42) at right angles to the incision in the external oblique aponeurosis. Blunt retractors should now be introduced into this in turn and the edges separated.

The transversalis fascia is thus well exposed and is then divided in the same line. Last of all the section of the peritoneum is made.

Two sets of retractors must be in use, one holding open the superficial wound from side to side, the other separating the edges of the deeper wound from above downward. A considerable opening is thus formed, through which, in suitable cases, the caput coli can be easily handled, and the appendix removed. The appendix having been taken away, the wound in the peritoneum, which is transverse, is then closed by suture. The similar wound in the fascia transversalis is also sutured. The fibers of the internal oblique and transversalis muscles fall together as soon as the retractors are withdrawn, and with a couple of fine catgut stitches the closure can be made more complete. The wound in the external oblique aponeurosis is sewed with catgut from end to end. When the operation is completed it will be seen that the gridiron-like arrangement of the muscular and tendinous fibers, to which the abdominal wall largely owes its strength, is restored almost as completely as if no operation had been done. In performing this operation I have noticed several advantages.

In the first place, muscular and tendinous fibers are separated, but not divided, so that muscular action cannot tend to draw the edges of the wound apart, but rather to actively approximate

them. Excepting during the incision of the skin, almost no bleeding occurs. The fascia transversalis not being drawn away by the retraction of the deepest layer of muscular fibers, this fascia is easily completely sutured, and thus greater strength of repair is assured. No muscular fibers or larger nerves having been divided, pain after operation is almost absent. The operation requires rather more time than the usual one, and a larger number of assistants is needed, for four retractors are in use during part of the time. The opening into the peritoneal cavity is not large, but may be made larger if necessary, by continuing (p. 43) the separation of the fibers of the internal oblique and transversalis, and dividing the conjoined aponeurosis in the same line with scissors. In the opposite direction the separation of muscular fibers may be carried out as far as the crest of the ilium.

I have now done this operation on four patients, all cases of recurrent appendicitis operated upon in the interval between attacks. The first operation took place at the Roosevelt Hospital on Dec. 18, 1893. Sufficient time has not elapsed to justify me in presenting the final results as positively an improvement upon those obtained by older methods. I shall expect, however, in these cases, a much more perfect result as regards the strength of the abdominal wall than is usually observed.

I present the method now, hoping that others may be induced to give it a trial.

This operation does not appear to be suitable for cases accompanied by suppuration about the appendix, which require to be treated by extensive packing with gauze, nor in cases non-suppurative which require during operation a large intra-abdominal dissection.

It is not an easy operation, and should not be attempted by those who are unfamiliar with operations upon the appendix, and I again call attention to the fact that in performing it two extra assistants will be occupied part of the time with retractors.

THE END

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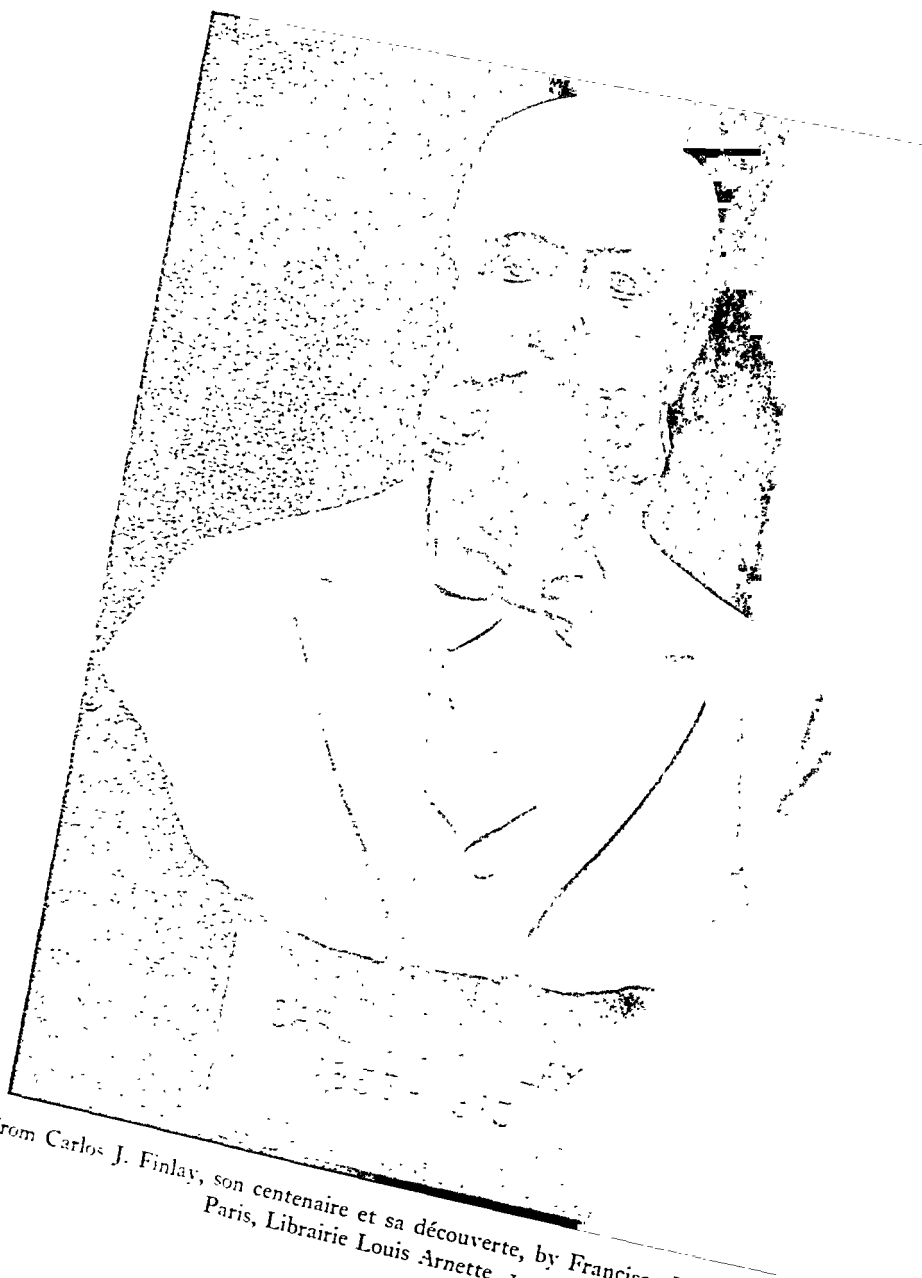
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From Carlos J. Finlay, son centenaire et sa découverte, by Francisco Dominguez,
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Carlos Juan Finlay

BIOGRAPHY

- 1833 Born December 3, in the city of Puerto Principe (now Camagüey), Cuba. His father, Edward, was a Scottish physician and his mother, Isabel de Barrés, was a native of France. Christened Juan Carlos, used Carlos as name, added J. as middle initial when his son, Carlos E., began practice of medicine. Family early moved to Havana and Guanamar where Edward Finlay had a coffee plantation.
- 1844 Age 11. Sent to France and entered a school at the Havre.
- 1846 Age 13. Returned to Cuba because of an attack of chorea which "left him with a serious stoppage in his speech which was cured after a careful course of training instituted by his father."
- 1848 Age 15. Returned to Europe. Because of revolutionary movements in France, studied in London for a time and then in Mentz on the Rhine for one year. Attended college in Rouen.
- 1851 Age 18. Returned to Cuba to convalesce from typhoid fever.
- 1855 Age 22. Graduated from the Jefferson Medical College of Philadelphia where his most influential teacher was Dr. John Kearsly Mitchell, an early worker in the germ theory of disease, and whose son, Dr. S. Weir Mitchell, was his private preceptor.
- 1856 Age 23. Practiced medicine for a short time with his father in Lima, Peru.

- 1857 Age 24. Incorporated his diploma in the University of Havana and began practice of medicine.
- 1860 Age 27. Visited Paris, attended hospital clinics.
- 1864 Age 31. Started a practice in Matanzas, near Havana, with general medicine and ophthalmic surgery.
- 1865 Age 32. Married in Havana, Miss Adela Shine, a native of the Island of Trinidad. "They have founded a family much esteemed in the social circles of Havana." One of his three sons is Carlos E. Finlay, M.D., F.A.C.S., a practicing physician in Havana.
- 1869 Age 36. Visited for several months in Trinidad.
- 1875 Age 42. Visited New York seeking medical aid for his wife.
- 1881 Age 48. First made public his views on the transmission of yellow fever by an intermediary agent at the International Sanitary Conference in Washington.
- 1898 Age 65. Became United States Army surgeon in Spanish-American War. Worked at Santiago.
- 1901 Age 68. Received Mary Kingsley medal from the Liverpool School of Tropical Medicine.
- 1902 Age 69. Appointed Chief Health Officer and President of the Superior Board of Health by the Cuban Government.
- 1905 Age 72. President of the 32nd session of the American Public Health Association held in Havana.
- 1908 Age 75. Made an officer of the Legion of Honor by the French Government.
Retired because of age from office of Chief of Sanitation.
- 1909 Age 76. Appointed Honorary President of the National Board of Sanitation and Charities at a salary of \$2,500.00 a year.
- 1911 Age 78. Elected a Corresponding Member of the French Academy of Medicine.
- 1915 Age 82. Died on August 20 in Havana.

Received LL.D. from Jefferson Medical College.
Honorary Fellow of the College of Physicians of Philadelphia.

Member of the Academy of Medical, Natural, and Physical Sciences of Havana.

Member of the "Sociedad de Estudios Clinicos."

BIBLIOGRAPHY OF WRITINGS

ABBREVIATIONS

- A. de la A. (Anales de la Real Academia de Ciencias Médicas. Físicas y Naturales de la Habana, y Anales de la Academia de Ciencias Médicas, Físicas y Naturales de la Habana).
 Arch. de Méd. Nav. (Archives de médecine navale).
 Arch. de la S. de E. C. de la H. (Archivos de la Sociedad de Estudios Clinicos de la Habana).
 Bol. de las D. ocurr. en el T. M. de la H. (Boletín de las Defunciones ocurridas en el Termino municipal de la Habana).
 C. M-Q. de la H. (Crónica Médico-Quirúrgica de la Habana).
 Gac. M. de la H. (Gaceta Médica de la Habana).
 Jour. Amer. Med. Assoc. (The Journal of the American Medical Association).
 La Enc. (La Enciclopedia).
 Prog. Méd. (El Progreso Médico).
 Rev. de C. M. (Revista de Ciencias Médicas).
 Rev. de M. y C. de la H. (Revista de Medicina y Cirugía de la Habana).
 Rev. Méd. Cub. (Revista Médica Cubana).
 Rev. de M. Trop. (Revista de Medicina Tropical).
 Rev. de la A. M-F. de la I. de C. (Revista de la Asociación Médico-Farmacéutica de la Isla de Cuba).
 Trab. de la Com. de M. L. é H. P. etc. (Trabajos de la Comisión de Medicina Legal é Higiene Pública de la Academia de Ciencias Médicas, Físicas y Naturales de la Habana, etc.).

1. Bocio exoftálmico. Observacion. (Exophthalmic goitre. Observation.) A. de la A. 1: 21-27, 1864.
2. El cólera y su tratamiento. (Cholera and its treatment.) Ibid., 2: 375-383, 1865.
3. Hernia ínguino-escrotal oblicua. Estrangulacion durante 41 horas. Vómitos estercoreos. Curacion. (Oblique

- inguinal-scrotal hernia. Strangulation for forty-one hours. Fecal vomiting. Cure.) Ibid., 3: 481-486, 1866.
4. Carta remitida al "Diario de la Marina" sobre el cólera en el Cerro. (Letter sent to the "Diario de la Marina" on cholera in Cerro.) Written June 27, 1868. Appears first time in Trabajos selectos del Dr. Carlos J. Finlay, Habana, pp. 575-578, 1912.
 5. Alcalinidad atmosférica observada en la Habana. (Alkalinity of the atmosphere observed in Havana.) A. de la A. 9: 183-192, 1872; 10: 42-46, 1873.
 6. Discusión del informe del Sr. Melero relativo á la explosión de una retorta en que se preparaba oxígeno. (Discussion of the report of Mr. Melero on the explosion of a retort in which oxygen was prepared.) Ibid., 9: 413, 1872.
 7. Transmisión del cólera por medio de las aguas corrientes cargadas de principios específicos. (Transmission of cholera by means of running water charged with the specific principle.) Ibid., 10: 159-170, 1873.
 8. Casos de tétanos tratados por el hidrato de cloral. (Case of tetanus treated by chloral hydrate.) Ibid., 10: 238, 1873.
 9. Explicación del cuadro de casos de cólera observados en el Cerro desde Noviembre 11, 1867, hasta Enero 29 de 1868. (Explanation of a list of cases of cholera observed at Cerro from Nov. 11, 1867 to Jan. 29, 1868.) Ibid., 11: 70-75, 1874.
 10. Consideraciones relativas á una observación interesante de cáncer y su tratamiento quirúrgico. (Considerations relative to an important observation on cancer and its surgical treatment.) Ibid., 11: 357-361, 1874.
 11. Nueva teoría de la gravitacion. (New theory of gravitation.) Ibid., 11: 429-441, 1874.
 12. Nota adicional á la "Nueva teoría de la gravitacion." (Additional note on the "New theory of gravitation.") Ibid., 11: 469-475, 1874.

13. Segundo informe relativo á la misma fábrica de jabón. (Second report on the manufacture of soap.) Trab. de la Com. de M. L. é H. P. etc., 3: 332-338, 1874. Also: A. de la A., 16: 286-288, 1874.
14. Informe sobre el pliego de condiciones á que ha de ajustarse la nueva empresa del alumbrado de gas de la Habana. (Report on the specifications for regulating the new enterprise of gas-lighting in Havana.) Trab. de la Com. de M. L. é H. P. etc., 3: 344-349, 1874. Also: A. de la A., 15: 165-166, 1878.
15. Informe acerca de la memoria "Aclimatacion é Higiene de los Europeos en Cuba." (Report on the account "Acclimation and hygiene of Europeans in Cuba.") A. de la A., 12: 66-84, 1875.
16. Consideraciones generales sobre la extracción de los cataratas y descripción de un nuevo método operatorio. (General considerations on the extractions of cataracts and description of a new operative method.) Ibid., 12: 285-298, 1875.
17. Observaciones de una extracción de catarata por su nuevo método operatorio y de una catarata congénita. (Observations on the extraction of cataract by a new operative method and of congenital cataract.) Ibid., 12: 339-342, 1875.
18. Informe sobre des obras de oftalmología. (Report on some works on ophthalmology.) Ibid., 12: 427-435, 1875.
19. La verdad científica, la invencion y su correctivo. (Scientific truthfulness, invention and accuracy.) Ibid., 13: 36-44, 1876.
20. Datos relativos á la corea: investigacion. (Data relative to chorea: investigation.) Ibid., 13: 247-248, 1876.
21. Patología y terapéutica del oparato lenticular del ojo por el professor Otto Becker de Heidelberg. (Pathology and treatment of the lenticular apparatus of the eye by Professor Otto Becker of Heidelberg.) Translation by Finlay from the German. 432 pp., 4°, Habana, G. Montial y Ca., 1876.

22. Oftalmología. Inconvenientes de la atropina. (Ophthalmology. Disadvantage of atropine.) A. de la A., 13: 495-504, 1876.
23. Crítica de la Memoria del Dr. Santos Fernández acerca de los "Trastornos del aparato de la visión en las fiebres palúdicas y accidentes á que puede dar lugar su ineludible tratamiento por el sulfato de quinina." (Criticism of the account of Dr. Santos Fernandez on the "Disturbances of visual apparatus in malaria and the accidents which may supervene in the unavoidable treatment with quinine.) Ibid., 14: 454-464; 509-513, 1877.
24. Informe sobre el Reglamento de la Sociedad Antropologica de la Isle de Cuba. (Report on the by-laws of the Anthropological Society of the island of Cuba.) Ibid., 14: 572, 1877.
25. Mocion del Dr. Finlay referente á los académicos penodistas. (Plan of Dr. Finlay in reference to the Academy of Journalists.) Ibid., 15: 179-182, 1878.
26. Clima de la isla de Cuba. (Higiene pública.) (Climate of Cuba. (Public Hygiene.)) Ibid., 15: 261-273, 1878.
27. Apología del clima de Cuba. (Apology of the climate of Cuba.) Gaz. M. de la H., 1: 1-3, 1878. Also: Rev. de med. y cirug. pract., Madrid, 3: 496-500, 1879.
28. Utilidad de los ejercicios comporales en los climas cálidos, y su conveniencia para formentar el desarrolo fisico de nuestra juventud. (Benefit of physical exercises in a warm climate and their advantages in the development of the physique of our young people.) Gac. M. de la H., 1: 116-117; 135-137, 1879.
29. Memoria sobre la etiología de la fiebre amarilla. (Account of the etiology of yellow fever.) Ibid., 1: 161-165; 177-181; 2: 7-9; 20-23, 1879; 2: 33-35; 53-59, 1880.
30. Addendum. Report of the alkalinity of the atmosphere observed in Havana and other localities of the island of Cuba. (Portion of report of the Havana Yellow Fever Commission. Spanish Commission.) Supplement Nat. Board of Health Bull., Washington, pp. 18-19, 1879.

Also, in Spanish: C. M-Q. de la H. 6: 375-380, 1880.
Also, in Spanish: Gac. M. de la H., 2: 158-160, 1880.

31. Informe acerca de un vendaje compresor binocular. (Report on a binocular compression bandage.) A. de la A., 16: 70, 1879.
32. Discusión sobre el tratamiento electroterápico del bocio exoftálmico. (Discussion of the electrotherapeutic treatment of exophthalmic goitre.) Ibid., 279-280, 1879.
33. Discusión del "Informe sobre secuestación de los lazarinos" del Dr. Nuñez. (Discussion on "The report on the segregation of lepers" by Dr. Nuñez.) Ibid., 16: 297-301, 1879.
34. Principios científicos de la electroterapia. (Scientific principles of electrotherapy.) Ibid., 16: 322-328, 1879.
35. Discusión del "Informe del Dr. J. J. Rovira sobre una fábrica de jabón." (Discussion on "The report of Dr. J. J. Rovira on the manufacture of soap.") Ibid., 16: 333-336, 1879.
36. Discusión del "Informe sobre secuestación de los lázaros" de Dr. José I. Torralbas. (Discussion on "The report on the segregation of lepers" by Dr. Jose I. Torralbas.) Ibid., 16: 363-371, 1879.
37. Higiene pública. La lepra. (Public hygiene. Leprosy.) Ibid., 16: 428, 1879.
38. Discusión del "Informe sobre secuestación de los lazarinos" del Dr. Tomás M. Govantes. (Discussion on "The report of segregation of lepers" by Dr. T. M. Govantes.) Ibid., 16: 471, 1879.
39. El mosquito hipotéticamente considerado como agente de transmisión de la fiebre amarilla. (The mosquito hypothetically considered as the agent of transmission of yellow fever.) (Read before the Royal Academy of Havana, Aug. 1881.) A. de la A., 18: 147-169, 1881. Also: Rev. de la A. M-F. de la I. de C., 2: 264-272; 354-362, 1902. Also, in English: Ibid., 273-281; 362-370. Also: 4°, Havana, 1902. Also: 30 pp., Mexico, A. Carranza y Comp., 1906.

40. Discusión del trabajo del Dr. Santos Fernández acerca de "La pérdida de la vista en la fiebre amarilla." (Discussion of the work of Dr. S. Fernández on "The loss of vision in yellow fever." A. de la A., 18: 212-213, 1881.
41. Moción del Dr. Finlay, para crear una comisión permanente de fiebre amarilla, Feb. 29, 1880. (Motion of Dr. Finlay, to create a permanent commission of yellow fever.) Arch. de la S. de E. C. de la H., 1: 103-105, 1881.
42. Reglamento para la Comisión del estudio de la fiebre amarilla. (Regulations for the commission for the study of yellow fever.) Arch. de la S. de E. C. de la H., 1: 133-136, 1881.
43. Comisión de fiebre amarilla. Estado de trabajos por ella ejecutados durante el pasado trimestre. (Commission of yellow fever. Account of the work performed by it during the past three months.) Ibid., 1: 182-184, 1881.
44. Notas acerca de la filaria hemática en los animales y en el hombre. (Notes on the Filaria hematic in animals and in man. A. de la A., 18: 373-376, 1881.
45. Patología vegetal. Enfermedad de los cocoteros. (Vegetable pathology. Disease of the cocoa tree.) Ibid., 18: 398-400; 405-406, 1881.
46. Communication of Dr. Finlay, on the transmission of yellow fever through an intermediary agent, to the International Sanitary Conference of Washington 1881. Inter. Sanitary Conf., Protocols of the proceedings No. 7: 108-110, 1881. Also, extract: A. de la A., 17: 449-495, 1880. Also, abstr.: Gac. M. de la H., 3: 175-177; 197-199; 218-219, 1881.
47. Informe reglamentario de la Comisión de fiebre amarilla. Pour su Presidente, el Dr. Carlos Finlay. (Regulatory report of the Commission of yellow fever. By the President, Dr. C. Finlay.) Arch. de la S. de E. C. de la H., 2: 98-109, 1882.
48. Consideraciones acerca de algunos casos de filariosis observados en la Habana. (Considerations of some cases of filariosis observed in Havana.) A. de la A., 19: 40-51, 1882.

49. Patogenia de la fiebre amarilla. (Pathogenesis of yellow fever.) Ibid., 160-178, 1882. Also: C. M.-Q. de la H., 9: 60-64; 119-125; 168-175, 1883.
50. Opinión de Finlay sobre la contagiosidad de la lepra. (Observations of Finlay on the contagiousness of leprosy.) A. de la A., 19: 184, 1882.
51. Histología. Consideraciones acerca de los estudios recientemente practicados sobre la hemoglobina y su medición con un espectro-fotómetro. (Histology. Consideration of recent practical studies on hemoglobin and its measurement with a spectro-photometer.) Ibid., 19: 302-305, 1882.
52. Exposición de Amsterdam; moción del Dr. Finlay, delegado de la Academia en la subcomisión habanera. (Exposition of Amsterdam; motion of Dr. Finlay.) Ibid., 19: 309-311, 1882.
53. Nuevos datos acerca de la relación entre la fiebre amarilla y el mosquito. (New data on the relation between yellow fever and the mosquito.) Ibid., 19: 455-466, 1882.
54. Opinión del Dr. Grancher sobre algunas preparaciones destinadas á comprobar la teoría patogénica de la fiebre amarilla. (Opinion of Dr. Grancher on some of the preparations designed to prove the pathogenic theory of yellow fever.) Ibid., 19: 487-489, 1882.
55. Correspondence. A monsieur le docteur A. Le-Roy de Méricourt, Directeur des Archives de Médecine Navale. (Correspondence. To Dr. A. Le-Roy de Mericourt.) Arch. de méd. nav., Paris, 39: 307-309, 1883.
56. Reseña de los experimentos de Grawitz y de Leber acerca de la inocuación de hongos microscópicos en el organismo animal. (Description of the experiments of Grawitz and Leber on the inoculation of microscopic amounts of toad-stool into animals.) A. de la A., 20: 154-161, 1883.
57. Informe acerca de una "Estadística médica demográfica de la ciudad de Barcelona durante el año 1882" y "Cuadro demográfico-sanitario-meteorológico de la ultima epidemia de sarampión observada en la antedicha ciudad (1881-1882)" remitidos por el Dr. José A. Nin y Pullés,

- en opción al título de académico corresponsal. (Report on "Vital statistics of the city of Barcelona in 1882" and "Sanitary, meteorological and vital statistics in the last epidemic of measles observed in that city (1881-1882)" transmitted by Dr. J. A. Nin y Pulles, candidate for corresponding membership.) Ibid., 20: 288-290, 1883.
58. Discusión con motivo de una nota traducida por el doctor Mestre acerca de la teoría parasitaria aplicada á las afecciones maláricas. (Discussion of an account submitted by Dr. Mestre on the parasitic theory of malarial affections.) Ibid., 20: 293-295, 1883.
59. Transmission experimental de la osteo-mielitis aguda, y deducciones relativas á la inoculación de la fiebre amarilla. (Experimental transmission of acute osteomyelitis, and deductions relative to the inoculation of yellow fever.) Ibid., 20: 379-383, 1883.
60. Reflexiones sobre la anestesia por el recto. (Reflections on anesthesia by rectum.) Ibid., 20: 552, 1883.
61. Comunicación relativa á la transmisión del agente colerígeno por el agua. (Communication relative to the transmission of the choleraform agent by water.) Ibid., 21: 168-169, 1884.
62. Opuntes sobre la historia primitiva de la fiebre amarilla. (Notes on the early history of yellow fever.) Ibid., 21: 265-291, 1884.
63. Hongo encontrado en la fiebre amarilla. (Toadstools disclosed in yellow fever.) Ibid., 21: 330, 1884.
64. Informe acerca de una memoria sobre fiebre amarilla con opción al título de Socio corresponsal. (Report concerning a memoir on yellow fever with choice of title of a corresponding member.) Ibid., 21: 401-414, 1884.
65. Objeciones hechas al bacilo colerígeno de Koch. (Objections made to the choleraform bacillus of Koch.) Ibid., 21: 466-473, 1884.
66. Consulta sobre el restablecimiento de la vista en un ojo á consecuencia de una lesión del otro. (Opinion on the restoration of eyesight following an injury to the opposite eye.) Ibid., 21: 504-505, 1884.

67. Periepecias del microbio del cólera. (Vicissitudes of the microbe of cholera.) Ibid., 21: 521-522, 1884.
68. Patogenia de la fiebre amarilla. (Pathogenesis of yellow fever.) Voz de Hipócrates, México, 2: 163-165, 1884.
69. Fiebre amarilla experimental, comparada con la natural en sus formas benignas. (Experimental yellow fever compared with the natural type in its benign forms.) C. M.-Q. de la H., 10: 51-67; 91-106, 1884. Also: Arch. de la S. de E. C. de la H., 12: 281-332, 1903. Also: 104 pp., 8°, Habana, 1904.
70. Contestación al discurso del Dr. D. Claudio Delgado: Investigaciones del Dr. Ferrán sobre el cólera. (Response to the discourse of Dr. D. C. Delgado on the investigations of Dr. Ferran on cholera.) A. de la A., 22: 39-89, 1885.
71. Nuevas consideraciones acerca de la historia de la fiebre amarilla. (New considerations of the history of yellow fever.) Ibid., 22: 104-124, 1885.
72. Estado sanitario de la Habana con relación á la fiebre amarilla. (Sanitary condition of Havana in relation to yellow fever.) Ibid., 22: 186-187, 1885.
73. Casos clínicos de "taenia solium" y su tratamiento. (Clinical cases of "tenia solium" and their treatment.) Ibid., 22: 284-286, 1885.
74. Casos de speticemia aguda y mortal á pesar de la profilaxis y el tratamiento antisépticos. (Cases of acute septicemia, fatal in spite of prophylaxis and antiseptic treatment.) Ibid., 22: 308-322, 1885.
75. Trichinosis. (Trichinosis.) La Enc., 1: 16-21; 63-69, 1885.
76. Trasplantación del ojo. (Transplantation of the eye.) Lancet, London, Dec. 15, 1885. Also: La Enc., 2: 35-36, 1886.
77. Hematimetria en la fiebre amarilla. (Hematimetry in yellow fever.) C. M.-Q. de la H., 11: 302-369, 1885.
78. Yellow fever; its transmission by means of the culex mosquito. Am. J. M. Sc., n.s. 92: 395-409, 1886.

79. ¿Beri-beri ó trichinosis? (Beri-beri or trichinosis?) La Enc., 2: 116-124, 1886.
80. ¿Trichinosis ó beri-beri? (Trichinosis or beri-beri?) Ibid., 2: 311-312, 1886.
81. Etiología del tétano traumático. (Etiology of traumatic tetanus.) Ibid., 2: 311-312, 1886.
82. Kakké, ó beri-beri del Japan. (Kakke or beri-beri in Japan.) Ibid., 2: 369-370, 1886.
83. La circulacion en el kakke. (The circulation in kakke (beri-beri).) Ibid., 2: 430-431, 1886.
84. La nitroglicerina en las enfermedades del corazón. (Nitroglycerin in diseases of the heart.) Ibid., 2: 585-586, 1886.
85. Opinion de Bérenger-Féraud sur "Le traitement des abces hépatiques." (Opinion of Bérenger-Féraud on "The treatment of hepatic abscess.") C. M.-Q. de la H., 12: 393, 1886. Also: Arch. de la S. de E. C. de la H., 3: 71-72, 1888.
86. Cultivos de sangre y otros productos de la fiebre amarilla. (Cultures of the blood and other products of yellow fever.) A. de la A., 23: 266-270; 346-349, 1886. Also: C. M.-Q. de la H., 12: 487-490, 1886. Also: La Enc., 2: 462-464, 1886. Also: Rev. Enciclo. de Cien. Méd., Fís. y Natur. de la H., 1: 155-157, 1886.
87. Cultivos de fiebre amarilla. (Cultures of yellow fever.) A. de la A., 23: 428, 1886.
88. Instalación de un laboratorio bacteriológico. By C. Delgado and Finlay. (Installation of a bacteriologic laboratory.) Ibid., 23: 492-501, 1886.
89. Investigaciones sobre fiebre amarilla. (Investigations concerning yellow fever.) Ibid., 24: 104-114, 1887. Also: Rev. de C. M., 20, July 30, 1887.
90. Relación entre los cultivos recientes de fiebre amarilla y los observados el año anterior. With C. Delgado. (Relation between recent cultures of yellow fever and those observed in the previous year.) A. de la A., 24: 166-169, 1887.

91. Colonias de tetrágenos sembrados por mosquitos. (Colonies of tetragenus spread by the mosquito.) Ibid., 24: 205-210, 1887.
92. Informe sobre las obras del Dr. A. Jacobí presentadas con opción al título de miembro corresponsal. (Report on the work of Dr. A. Jacobí, presented as a candidate for corresponding membership.) Ibid., 24: 210-217, 1887.
93. Del micrococo tetrágeno de la fiebre amarilla. (The micrococcus tetragenus of yellow fever.) With C. Delgado. Ibid., 24: 434-446, 1887. Also, abstr.: Rev. de C. M. 32, Feb. 20, 1888.
94. Refutación al Dr. Gibier de las explicaciones dadas acerca de un tubo bacteriológico sembrado por el mismo. (Refutation to Dr. Gibier on the explanation given the subject of a bacteriologic tube sown by himself.) By C. Delgado and Finlay. A. de la A., 24: 461-477, 1887. Also, abstr.: Rev. de C. M., 33, Mar. 5, 1888.
95. Relación entre los factores etiológicos y la evolución de la fiebre amarilla. (Relation between the etiologic factors and the evolution of yellow fever.) A. de la A., 24: 537-546, 1887. Also: Rev. de C. M., 34, Mar. 20, 1888.
96. Resumen de las investigaciones sobre tetrágenos en la fiebre amarilla. (Resumé of the researches on the tetragenus in yellow fever.) With C. Delgado. A. de la A., 24: 590-601, 1887. Also: Rev. de C. M., 38, May 20, 1888.
97. Contestación al Dr. Tamayo. (Reply to Dr. Tamayo.) With C. Delgado. Rev. de C. M., 25, Oct. 15, 1887.
98. Etiología y profilaxis de la fiebre amarilla; estudio comparativo de los trabajos últimamente realizados sobre la materia. (Etiology and prophylaxis of yellow fever; comparative study of the work ultimately accomplished on the subject.) With C. Delgado. 14 pp., 1 p., 8°, Habana, 1887.
99. Estado actual de nuestros conocimientos, tacante á la fiebre amarilla. (Actual state of knowledge of yellow fever.) La Enc., 3: 102-105; 435-443, 1887. Also: Imp. La Propaganda Literaria. Habana, 1887.

100. The microbe of yellow fever. *Medical Record*, N. Y., 33: 622, 1888.
101. The bacteriology of yellow fever. *Lancet*, Lond., 2: 445-446, 1888. Also in Spanish: *Rev. de C. M.*, 46, Sept. 20, 1888.
102. Comunicación sobre el micrococcus febris flavae. (Communication on the micrococcus febris flavae.) With C. Delgado. *A. de la A.*, 25: 276-278; 458, 1888. Also, abstr.: *Rev. de C. M.*, 47, Oct. 5, 1888.
103. Resumen de nuestras investigaciones sobre etiología de la fiebre amarilla en el año de 1888 á 1889. (Resumé of our researches on the etiology of yellow fever during the year 1888 to 1889.) With C. Delgado. *A. de la A.*, 25: 739-753, 1888. Also, abstr.: *Rev. de C. M.*, 4: 76-78; 91-92, 1889.
104. Sur le micrococcus versatilis (Sternberg). (On the micrococcus versatilis (Sternberg).) By C. Delgado and C. Finlay. *J. de l'anat. et physiol.*, 25: 223, 1889.
105. Diagnóstico bacteriológico del muermo. (Bacteriologic diagnosis of glanders.) *Rev. de C. M.*, 4: 138-139, 1889.
106. Opinion personnelle du Docteur Finlay sur un rapport de Docteur Tamayo sur trois chevaux malades de la morve. . . (Personal opinion of Dr. Finlay on Dr. Tamayo's report of three horses ill with glanders. . .) *Rev. de la C. M.*, 4: 176-179, 1889. Also: *A. de la A.*, 26: 238-243, 1889.
107. Resultado de los experimentos comparativos hechos sobre el micrococco "tetragenus versatilis." (Result of comparative experiences made on the micrococcus "Tetragenus versatilis.") With C. Delgado. *A. de la A.*, 26: 739-753, 1889. Also, abstr.: *Rev. de C. M.*, 5: 130, 1889.
108. Estadística de las inoculaciones con mosquitos contaminados en enfermos de fiebre amarilla. (Statistics of inoculations made with mosquitoes contaminated with the disease of yellow fever.) With C. Delgado. *A. de la A.*, 27: 459-469; 501-519, 1890. Also: *Rev. de C. M.*, 5: 294-295, 1890. Also: 33 pp., 8°, Habana, Alvarez, 1891.

109. Investigación experimental sobre la linfa del Dr. Koch. (Experimental investigation of the lymph of Dr. Koch.) With C. Delgado. *Ibid.*, 27: 737-744, 1890.
110. Inoculation by mosquitoes against yellow fever. Boston M. & S. J., 124: 273, 1891. Also: *Lancet*, London, Jan. 31, 1891. Also, in Spanish: *Rev. de C. M.*, 1891.
111. Inoculation for yellow fever by means of contaminated mosquitoes. *Am. J. Med. Sc.*, 102: 264-268, 1891.
112. Comunicación acerca de un nuevo recurso terapéutico en el tratamiento de la fiebre amarilla. (Communication on the subject of a new therapeutic method in the treatment of yellow fever.) *A. de la A.*, 29: 202-209, 1892. Also: *Rev. de C. M.*, 7: 181-183, 1892.
113. Yellow fever, before and after the discovery of America. *Climatologist*, Phila., 2: 338-349, 1892.
114. Tratamiento del cólera. (Treatment of cholera.) *Prog. Méd.*, 4: 295-299, 1892. Also: *Arch. de la S. de E. C. de la H.*, 5: 331-338, 1895.
115. Concordancia entre la filología y la historia en epidemiología primitiva de la fiebre amarilla. (Concordance between the philology and the history in a primitive epidemic of yellow fever.) 28 pp., 4°, Merida de Yucatan, Imp. Mercantil, 1892. Also: *C. M.-Q. de la H.*, 23: 167-182, 1897. Also: 16 pp., 8°, Habana, 1897.
116. Yellow fever immunity. Modes of propagation. Mosquito theory. *Comptes Rendus et Memoires du Huitieme Congres International d'Hygiene et de Demographie*, tenu a Budapest du 1 au 9 Septembre 1894, pp. 702-706.
117. Patología médica. Fiebre amarilla en los criollos. (Medical pathology. Yellow fever among creoles.) *A. de la A.*, 31: 190-191, 1894.
118. Yellow fever. *Edinburgh M. J.*, 40: 35-45; 328-335; 414-421, 1894. Also, in Spanish: *C. M.-Q. de la H.*, 21: 143-151; 171-178; 202-205; 226-233; 255-260, 1895. Also: 30 pp., 4°, Habana, Alvarez, 1895.

119. The "tetragonococcus" or "tetracoccus versatilis" and yellow fever. Edinb. M. J., 41: 513-529, 1895. Also: 18 pp., 8°, Edinburgh, Oliver & Boyd, 1895. Same, in Spanish: A. de la A., 32: 225-245, 1896. Same, abstr.: Prog. Méd., 6: 175-178, 1894.
120. Fiebre amarilla. Estudio clínico, patológico y etiológico. (Yellow fever. A clinical, pathologic and etiologic study.) 36 pp., 8°, Habana, imp. de Alvarez y Ca., 1895.
121. Comunicación acerca de un caso de "fiebre de borras" en que pudo comprobarse la presencia del "Tetracoco versatil." (Communication on the subject of a case of "fiebre de borras" in which the presence of "Tetracoccus versatilis" was proved.) Rev. de C. M., 10: 243-244, 1895. Also: A. de la A., 32: 299-303, 1896.
122. Nota sobre el diagnostico precoz, en un caso de fiebre amarilla. (Note on the early diagnosis in a case of yellow fever.) A. de la A., 32: 303-305, 1896.
123. Apéndice á la comunicacion sobre el tetracoco versatil y la fiebre amarilla. (Supplement to the communication on tetracoccus versatilis and yellow fever.) 8 pp., 8°, Habana, 1896.
124. La nueva tuberculosis (tuberculina) de Koch y algunos germenos que suele contener. (The new tuberculin of Koch and some germs which it may contain.) With J. N. Dávalos. A. de la A., 34: 234-239, 1897.
125. A plausible method of vaccination against yellow fever. Philadelphia Med. Jour., 1: 1123 only, 1898.
126. Los mosquitos considerados como agentes de transmisión de la fiebre amarilla y de la malaria. (The mosquito considered as the agent of transmission of yellow fever and of malaria.) A. de la A., 35: 31-32, 1899. Also: New York Med. Rec., 45: 737-739, 1899. Also: Rev. de la A. M-F. de la I. de C., 2: 350-354, 1902.
127. Etiología de la infección hemogastrica en la fiebre amarilla. (Etiology of hemogastric infection in yellow fever.) A. de la A., 36: 183-190, 1899. Also: Rev. de M. y C. de la H., 5: 117-122, 1900.

128. Gelbes Fieber. (Yellow fever.) In Handbuch der praktischen Medicin. 5: 486, 1900. Same, 2. ed., 4: 295-299, 1906.
129. Transmisión de la fiebre amarilla. (Transmission of yellow fever.) Rev. de la A. M-F. de la I. de C., 1: 373-376, 1901. Also: Jour. Amer. Med. Assoc., 36: 1040-1041, 1901.
130. Fiebre amarilla infantil. (Yellow fever in infants.) Rev. de M. Trop., 2: 97-99, 1901. Also, in: Nothnagel's Specielle Pathologie und Therapie, V Band, IV Theil, II Abtheilung.
131. Ensayo del suero caldas-bellinzaghi. (Testing of the serum caldas-bellinzaghi.) By Guiteras, Finlay, Albertini and Agramonte. Rev. de M. Trop., 2: 141-145, 1901.
132. Dos maneras distintas de transmitirse la fiebre amarilla por el culex mosquito (Stegomyia taeniata). (Two distinct means of transmission of yellow fever by the culex mosquito (Stegomyia taenia).) Ibid., 2: 185-192, 1901. Also: Jour. Amer. Med. Assoc., 37: 1387-1389, 1901.
133. Piezas constitutivas de la trompa del culex mosquito. (Parts constituting the proboscis of the culex mosquito.) Arch. de la S. de E. C. de la H., 11: 224-232, 1901. Also: Rev. de M. Trop., 3: 3-10, 1902.
134. Is the mosquito the only agent through which yellow fever is transmitted? Republic of Cuba. Sanitary Dept. of Havana. 8 pp., 4°, 1902. Also: Trans. 1st Gen. Internat. Sanitary Con. of Amer. Repub., Washington, pp. 67-71, 1903. Also: Rev. de la A. M-F. de la I. de C., 3: 245-250, 1903.
135. Method of stamping out yellow fever suggested since 1899. Republic of Cuba. Sanitary Dept. of Havana, 7 f., 4°, 1902. Also: Medicine, Mar., 1903. Also: Rev. de la A. M-F. de la I. de C., 3: 179-185, 1903.
136. Reseña de los progresos realizados en el siglo xix en el estudio de la propagación de la fiebre amarilla. Tercer Congreso Médico Pan-Americano. Actas de las sesiones y Memorias presentadas. (Review of the progress made

119. The "tetragonococcus" or "tetracoccus versatilis" and yellow fever. Edinb. M. J., 41: 513-529, 1895. Also: 18 pp., 8°, Edinburgh, Oliver & Boyd, 1895. Same, in Spanish: A. de la A., 32: 225-245, 1896. Same, abstr.: Prog. Méd., 6: 175-178, 1894.
120. Fiebre amarilla. Estudio clínico, patológico y etiológico. (Yellow fever. A clinical, pathologic and etiologic study.) 36 pp., 8°, Habana, imp. de Alvarez y Ca., 1895.
121. Comunicación acerca de un caso de "fiebre de borras" en que pudo comprobarse la presencia del "Tetracoco versatil." (Communication on the subject of a case of "fiebre de borras" in which the presence of "Tetracoccus versatilis" was proved.) Rev. de C. M., 10: 243-244, 1895. Also: A. de la A., 32: 299-303, 1896.
122. Nota sobre el diagnostico precoz, en un caso de fiebre amarilla. (Note on the early diagnosis in a case of yellow fever.) A. de la A., 32: 303-305, 1896.
123. Apéndice á la comunicacion sobre el tetracoco versatil y la fiebre amarilla. (Supplement to the communication on tetracoccus versatilis and yellow fever.) 8 pp., 8°, Habana, 1896.
124. La nueva tuberculosis (tuberculina) de Koch y algunos germenos que suele contener. (The new tuberculin of Koch and some germs which it may contain.) With J. N. Dávalos. A. de la A., 34: 234-239, 1897.
125. A plausible method of vaccination against yellow fever. Philadelphia Med. Jour., 1: 1123 only, 1898.
126. Los mosquitos considerados como agentes de transmisión de la fiebre amarilla y de la malaria. (The mosquito considered as the agent of transmission of yellow fever and of malaria.) A. de la A., 35: 31-32, 1899. Also: New York Med. Rec., 45: 737-739, 1899. Also: Rev. de la A. M-F. de la I. de C., 2: 350-354, 1902.
127. Etiología de la infección hemogastrica en la fiebre amarilla. (Etiology of hemogastric infection in yellow fever.) A. de la A., 36: 183-190, 1899. Also: Rev. de M. y C. de la H., 5: 117-122, 1900.

128. Gelbes Fieber. (Yellow fever.) In Handbuch der praktischen Medicin. 5: 486, 1900. Same, 2. ed., 4: 295-299, 1906.
129. Transmisión de la fiebre amarilla. (Transmission of yellow fever.) Rev. de la A. M-F. de la I. de C., 1: 373-376, 1901. Also: Jour. Amer. Med. Assoc., 36: 1040-1041, 1901.
130. Fiebre amarilla infantil. (Yellow fever in infants.) Rev. de M. Trop., 2: 97-99, 1901. Also, in: Nothnagel's Specielle Pathologie und Therapie, V Band, IV Theil, II Abtheilung.
131. Ensayo del suero caldas-bellinzaghi. (Testing of the serum caldas-bellinzaghi.) By Guiteras, Finlay, Albertini and Agramonte. Rev. de M. Trop., 2: 141-145, 1901.
132. Dos maneras distintas de transmitirse la fiebre amarilla por el culex mosquito (*Stegomyia taeniata*). (Two distinct means of transmission of yellow fever by the culex mosquito (*Stegomyia taenia*.) Ibid., 2: 185-192, 1901. Also: Jour. Amer. Med. Assoc., 37: 1387-1389, 1901.
133. Piezas constitutivas de la trompa del culex mosquito. (Parts constituting the proboscis of the culex mosquito.) Arch. de la S. de E. C. de la H., 11: 224-232, 1901. Also: Rev. de M. Trop., 3: 3-10, 1902.
134. Is the mosquito the only agent through which yellow fever is transmitted? Republic of Cuba. Sanitary Dept. of Havana. 8 pp., 4°, 1902. Also: Trans. 1st Gen. Internat. Sanitary Con. of Amer. Repub., Washington, pp. 67-71, 1903. Also: Rev. de la A. M-F. de la I. de C., 3: 245-250, 1903.
135. Method of stamping out yellow fever suggested since 1899. Republic of Cuba. Sanitary Dept. of Havana, 7 f., 4°, 1902. Also: Medicine, Mar., 1903. Also: Rev. de la A. M-F. de la I. de C., 3: 179-185, 1903.
136. Reseña de los progresos realizados en el siglo xix en el estudio de la propagación de la fiebre amarilla. Tercer Congreso Médico Pan-Americano. Actas de las sesiones y Memorias presentadas. (Review of the progress made

- in the 19th century in the study of the propagation of yellow fever.) Habana. 1: 195-211, 1902. Also, incomplete: Rev. de M. Trop., 2: 56-63, 1901.
137. Agreement between the history of yellow fever and its transmission by the culex mosquito (*Stegomyia* of Theobald). Jour. Amer. Med. Assoc., 38: 993-996, 1902.
 138. Cartas estadísticas del Dr. Carlos J. Finlay. (Statistical letters of Dr. Finlay.) Informe Sanitario y Demográfico de la República de Cuba. May 1902-Dec. 1908.
 139. Concepto probable de la naturaleza y el ciclo vital del germen de la fiebre amarilla. (Probable nature and life-cycle of the yellow fever germ.) Rev. de M. Trop., 4: 49-54, 1903. Also, in English: 13 pp., 4°, 1903.
 140. The transmission of yellow fever. Letter. Jour. Amer. Med. Assoc., 40: 1659-1660, 1903.
 141. Fiebre amarilla experimental según la técnica moderna. (Yellow fever according to the modern technique.) Arch. de la S. de E. C. de la H., 12: 406-444, 1903. Also: Rev. Méd. Cub., 4: 47-79; 160-161, 1904.
 142. Transmission de la fièvre jaune par le moustique culex. Manuscript de 1891. (Transmission of yellow fever by the culex mosquito. Manuscript of 1891.) Rev. de M. Trop., 4: 134-143, 1903.
 143. New aspects of yellow fever etiology, arising from the experimental findings of the last three years. Rev. de la A. M-F. de la I. de C., 3: 477-480, 1903. Also: Jour. Amer. Med. Assoc., 42: 430-431, 1904. Also: C. M-Q. de la H., 30: 11-13, 1904.
 144. Yellow fever: historical sketch of the disease, its etiology and mode of propagation. Reference Handbook of Med. Sc., 8: 322-332, 1904.
 145. Los leucocitos. Sugestiones acerca del papel que representan en la nutrición celular y en la formación de toxinas, lisinas, etc., y de los respectivos anticuerpos. (The leucocytes. Suggestions on the rôle which they play in cellular nutrition and in the formation of toxins, lysins,

- etc., and the respective antibodies.) A. de la A., 41: 82-91; 102-108, 1904.
146. Nota ampliativa de mi trabajo sobre "Los leucocitos." (Supplementary note on my work on "The leucocytes." Ibid., 41: 128-129. Also: Rev. Méd. Cub., 5: 1-17, 1904.
 147. Manual de practica sanitaria para uso de jefes e inspectores de sanidad, medicos, funcionarios, etc., de la Republica de Cuba. (Manual of practical sanitation for the use of chiefs and inspectors of sanitation, doctors, etc. of the Republic of Cuba.) xvi., 1114 pp., 22½ cm., Habana, 1905.
 148. Estado sanitario de la Isla de Cuba despues de la proclamación de la República. (Sanitary conditions on the islands of Cuba after the proclamation of the Republic.) Rev. de M. Trop., 6: 1-9, 1905.
 149. President's address. American Public Health Association, Havana, Cuba, 1905. Ann. Report Amer. Pub. Health Assoc., 1905.
 150. Casos de fiebra amarilla en la Habana en Octubre de 1905. La fiebre amarilla en la Habana. (Case of yellow fever in Havana in October, 1905. Yellow fever in Havana.) Bol. de las D. ocurr. en el T. M. de la H., Oct.-Dec., 1905. Also: Rev. de M. Trop., 7: 6-16, 1906.
 151. Nota preliminar sobre la importancia de ciertos factores secundarios en la mortalidad y transmisibilidad de la tuberculosis pulmonar. (Preliminary note on the importance of certain secondary factors in mortality and transmission of pulmonary tuberculosis.) Actos y Trabajos del Primer Congreso Médico Nacional. Habana. pp. 434-435, May 20-23, 1905.
 152. Importancia de ciertos factores secundarios en el desarrollo de la tuberculosis pulmonar y en la mortalidad producida por la misma. (Importance of certain secondary factors in the development of pulmonary tuberculosis and in the mortality produced by that disease.) A. de la A., 42: 62-76, 1905. Also: Rev. de M. Trop., 6: 97-109, 1905.

153. Del mosquito como factor etiológico de la fiebre amarilla. (The mosquito as the etiologic factor in yellow fever.) *Rev. Méd. Cub.*, 9: 3-8, 1906. Also: *Arch. de la S. de E. C. de la H.*, 13: 140-147, 1907. Also: *C. M-Q. de la H.*, 33: 232-234, 1907.
154. Casos, al paracer, típicos de íctero catarral simple como secuela posible de ataques benignos é ignorados de fiebre amarilla. (A case presenting the appearance of typical, simple, catarrhal jaundice, possibly the result of a benign and undiagnosed attack of yellow fever.) *A. de la A.*, 43: 202-205, 1907. Also: *Rev. de M. y C. de la H.*, 12: 45-50, 1907.
155. Atmospheric temperature as an essential factor in the propagation of yellow fever. XIV Internat. Congr. Hyg. & Demography, Berlin, 1907. Havana, Printing Office, 1907. Also, in Spanish: *Rev. Méd. Cub.*, 12: 130-147, 1908.
156. Discurso leído por el Dr. Carlos J. Finlay en el Aula Magna de la Universidad de la Habana, al recibir la medalla "Mary Kingsley." (Discourse read by Dr. Carlos J. Finlay in the Great Amphitheatre of the University of Havana, when he received the "Mary Kingsley" medal.) *Boletín oficial del Departamento de Estado de la Secretaría de Estado y Justicia. Habana.* 4: 338-339, 1907.
157. Discurso de gracias del doctor Carlos J. Finlay (Officier de la Orden la Légion de Honor (France).) (Discourse of thanks by Dr. Finlay.) *A. de la A.*, 45: 356-360, 1908.
158. Trabajos selectos del Dr. Carlos J. Finlay. (Selected papers of Dr. Carlos J. Finlay.) Habana, 1912. xxxiv, 657 pp., port., 26 cm., Spanish and English.

BIBLIOGRAPHY OF BIOGRAPHIES

- Biography by F. Grande Rossi. *Higiene, Habana*, 3: 149-152, 1893-4.
- Biography by B. Lee. *Escuela de Med., México*, 20: 98-106, 1905.
- Biography by J. Guiteras. *Rev. Méd. Cub., Habana*, 10: 233-247, 1907.

- Biography. Rev. de M. y C. de la H., 13: 549-552, 1908.
- Biography. A. de la A., 45: 343, 1908-9.
- Informe acerca de los trabajos científicos del Dr. Carlos J. Finlay.
By C. Delgado and J. LeRoy. Ibid., 45: 214-237.
- The work of Finlay in respect of insect borne disease. By J. Guiteras. Lancet, Lond., 1: 1715, 1910.
- El Dr. Carlos J. Finlay. By Juan Guiteras. 12 pp., 8°, Habana, Sierra, 1912.
- Biography by W. C. Gorgas. Am. J. Pub. Health, 5: 1177, 1915.
- Biography. Boston M. & S. J., 173: 444, 1915.
- Biography. Brit. M. J., 2: 626, 1915.
- Biography by E. B. Barnet. California State J. M., 13: 476-478, 1915.
- Biography by J. Santos Fernández. C. M.-Q. de la H., 41: 209-212, 1915.
- Biography. Med. Rec., 88: 366, 1915.
- Biography. J. A. M. A., 65: 814, 1915.
- Biography by A. Agramonte. New Orleans M. & S. J., 69: 55-60, 1915.
- Biography. New York M. J., 102: 468, 1915.
- Biography by J. LeRoy. Rev. de M. y C. de la H., 20: 349-354, 1915.
- Biography. Vida Nueva, Habana, 7: 170-178, 1915.
- Dr. Carlos J. Finlay. Address delivered by W. C. Gorgas, at the 43d annual meeting of the American Public Health Association, Rochester, N. Y., Sept. 7, 1915. 2 l., 4°, n.p., 1915.
- Dr. Carlos J. Finlay's positive cases of experimental yellow fever.
By C. E. Finlay. New Orleans M. & S. J., Nov. 1916.
- Biography by A. Agramonte. Tr. Am. Soc. Trop. Med., N. Orl., 10: 26-31, 1916.
- Carlos Finlay on the house mosquitoes of Habana. By F. Knob. Proc. Pan-Am. Scient. Cong., 1915-16, Wash., 9: 107-110, 1917.
- Biography. San. y Benefic. Bol. Ofic., Habana, 20: 1-197, 1918.
- Inauguración del monumento erigido a Finlay en la Secretaría de sanidad y beneficencia el 25 de marzo de 1916; alocución del

- Senor Secretario de Sanidad y Beneficenciz. By E. Nuñez. Ibid., 20: 105-107.
- Discurso pronunciado en la ceremonia del descubrimiento del busto del Dr. Carlos J. Finlay. By A. Agramonte. Ibid., 20: 112-116.
- Same. By J. Guiteras. Ibid., 20: 117-123.
- Dr. Osler's address on "The Nation and the tropics" and Dr. Finlay. By J. Guiteras. Ibid., 20: 124-128.
- Biography. American Review of Reviews. p. 386, Apr. 1920.
- Biography. New Orleans M. & S. J., 74: 222, 1921.
- Ein Denkmal für Carlos Finlay in Habana. By W. Hoffman. Berl. klin. Wochenschr., 58: 1231, 1921.
- Monument to Carlos Finlay in Havana. J. A. M. A., 77: 1113, 1921.
- Ein Aerztedenkmal. By C. Schilling. Deutsche med. Wochenschr., 47: 1433, 1921.
- Biography. M. J. & Rec., 120: 605-606, 1924.
- En Honor de Finlay. Bol. Ofic. san. panam., 7: 991, 1928.
- Finlay and his discovery of transmission of yellow fever by a mosquito. By J. Silverio Sainz. San. y benefic., 33: 623-634, 1928. Also: Actas y trab. del primer Cong. de la Asoc. med. Panamericana, pp. 114-128, 1930.
- Discovery of yellow fever agent. By J. Silverio Sainz. Rev. Méd. Cub., 40: 271-284, 1929.
- Review of work of Finlay and of Noguchi on yellow fever. By F. Berrios. San. y benefic., 34: 333-346, 1929.
- Biography. Portrait. Med. Rev. of Rev., 25: front., 1929.
- His fundamental work. By J. LeRoy y Cassá. Rev. Méd. Cub., 42: 1261-1274, 1931. Also: Gac. M. de México, 63: 165-177, 1932.
- Participation of author in efforts to compile Finlay's work on his discovery of yellow fever agent. By C. M. Garcia. C. M. Q. de la H., 58: 303-336, 1932.
- Centenary of birth; suggestion to celebrate his birthday as Pan-American day of Medicine. By H. Abascal. Rev. de M. y C. de la H., 38: 260-266, 1933. Also: Vida Nueva, 33: 47-53, 1934.

- Centenary of birth. By A. Leao Velloso. *Rev. de M. y C. de la H.*, 38: 546-548, 1933.
- Centenary of birth. By M. S. Iglesias. *Rev. Méd. Veracruzana*, 13: 1013-1019, 1933.
- Definition of Finlayism. By F. Miranda. *Ibid.*, 13: 1019-1021.
- Work in combating yellow fever. By E. Landa. *Ibid.*, 13: 1021-1030.
- Celebration of centenary of birth. By F. Dominguez. *Bull. Acad. de méd., Paris*, 110: 596-622, 1933. Also, *abstr.: Gaz. d. hôp.*, 106: 1741-1743, 1933.
- Centenary of birth; celebration at Academy of Medicine (*Le centenaire de Finlay a l'Académie de Médecine.*) *Vie méd.*, 14: 1065-1066, 1933.
- Celebration of centenary of birth at Academy of Medicine, Paris. By P. Desfosses. *Presse méd.*, 41: 2049, 1933.
- Remarks on yellow fever in honor of centenary of birth. By W. H. Hoffmann. *Rassegna internaz. di clin. e terap.*, 14: 1213-1220, 1933.
- Número especial dedicado al centenario del natalicio del Dr. Carlos J. Finlay. *C. M-Q. de la H.*, 59, 1933.
- Importance of work on transmission of diseases by insects. By L. O. Howard. *Ibid.*, 59: 511-512, 1933.
- Biography by C. M. Garcia. *Ibid.*, 59: 517-521, 1933.
- Biography by J. Guiteras. *Ibid.*, 497-504, 1933.
- Meeting of Academia Nacional de Medicina de México to honor Carlos Juan Finlay on centenary of birth and to celebrate Pan-American Day of Medicine. By S. Iturbide Alvírez. *Gac. Méd. de México*, 65: 41-51, 1934.
- Work as clinician. By F. Dominguez. *Rev. de M. y C. de la H.*, 40: 737-743, 1935.
- Docteur Carlos J. Finlay, son centenaire (1933), sa découverte (1881). By Francisco Dominguez. 302 pp., Paris, 1935.
- Life and work. By S. Garcíá Marruz. *Rev. Méd. Cub.*, 47: 106-122, 1936.
- Yellow fever; means of transmission; reminiscences of work of my father. By C. E. Finlay. *Bull. Am. Coll. Surgeons*, 21: 100-101, 1936.

Can the world still be ignorant of Finlay's great work, especially in relation to transmission of yellow fever? By L. Pastor Guesada. C. M-Q. de la H., 62: 566-571, 1936.
 Speech in his honor given on Day of American Medicine, Dec. 3, 1936. By A. Recio. Rev. de M. y C. de la H., 41: 727-738, 1936.

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INTRODUCTION

Yellow fever is a disease of tropical and sub-tropical countries, characterized by fever with jaundice, toxemia and albuminuria, and a tendency to hemorrhage, especially from the stomach.

This disease has been prevalent since the days of early history in the West Indies, in countries bordering on the Caribbean Sea, and on the west coast of Africa. Occasionally it has extended to the southern region of the United States, especially along the Atlantic seaboard. Serious epidemics of yellow fever have occurred as far north as Boston. Perhaps the most famous and serious attack of this disease in the United States took place in Philadelphia in 1793. In that city of 40,000 people, over 4,000 died in the period from August through November. Severe epidemics occurred in the United States occasionally throughout the 19th century and as late as 1903 a severe epidemic occurred in Texas near the Mexican Border.

Yellow fever has always been prevalent in Cuba. On that Island there was born in 1833 Carlos J. Finlay to whom goes the credit for first insisting that yellow fever was spread by mosquitoes. After being educated on the continent and in the United States, Finlay returned to his home in 1864, at the age of 31, and started a medical practice. Finlay's interest in yellow fever undoubtedly began at the time when he first realized that there was such a disease. We find him during his first year of medical practice gathering data on the climate of Havana. He was searching for a possible explanation of the mysterious outbreaks of yellow fever which occurred most seriously among white visitors to the Island. The natives had some immunity but nearly every foreigner contracted the disease within a year or two after arrival. Finlay noticed that when a boat anchored in the harbor of Havana and only the captain and mate came ashore, the crew being left aboard because of fear of contracting disease, nevertheless yellow fever broke out among the crew some time after the return of the captain and mate, even though these people continued in perfect health. Boats loaded at Havana sailed away to not-too-distant ports with their holds sealed. On arrival at a suitable and favorable port an epidemic of yellow fever broke out after the hold was opened. Finlay noticed also that yellow fever decreased when the temperature dropped to 50 or 60 degrees and the disease entirely disappeared when the freezing point was reached.

Dr. Finlay attempted to find one cause of the transmission of yellow fever which would explain all these startling facts. He probably thought first of personal and inanimate objects which had been in contact with patients (fomites). But transmission by these objects could not explain all the phenomena. Next Finlay considered flies as the go-between but this idea also had to

be discarded. Then this tireless worker decided that the mosquito was the agent of transmission of yellow fever.

The following pages of Finlay's writings show the problem which he had set himself. In the first place, he had to find out all he could about mosquitoes existing in Cuba. Then he had to allow certain mosquitoes to bite patients ill with yellow fever and later these same mosquitoes to bite volunteer patients. Finlay very early decided, and correctly so, that the species of mosquito responsible for the transmission was the *Culex Cubensis*, later called the *Stegomyia Fasciatus*, and still more recently *Aedes Egypti*. But read in his own words, published in 1881, the story of Finlay's inspiration and the experiments he performed to prove the truth of his idea.

Unfortunately, Finlay never produced an undoubted case of yellow fever in his experimental subjects. It has since been found that an infected mosquito requires about twelve days after biting a patient ill with yellow fever before it can give the disease to a second victim. This fact escaped Finlay but does not detract from the greatness of his imagination.

When the Yellow Fever Commission of the United States Army was sent to Cuba in the last years of the 19th century their leader, Major Walter Reed, conferred with Carlos J. Finlay on the mosquito theory of transmission. At that time the *Bacillus icteroides* of Sanarelli (*Bacillus X* of Sternberg) was considered the causative agent. Reed and his Commission soon showed that this bacillus was not the culprit and proceeded to test Finlay's mosquito theory. The story of Reed and his Commission (James Carroll, Aristide Agramonte and Jesse W. Lazear who lost his life) is a famous story which must be deferred until a further time. The Commission proved that yellow fever is conveyed by the mosquito and within a year Major William C. Gorgas was eradicating yellow fever from Cuba by isolating patients ill with this disease and eliminating the mosquitoes. In three months Havana was free from the disease for the first time in 150 years. Gorgas later applied the same methods of control of yellow fever and other infectious diseases in the Panama Canal Zone and made it possible for the Canal to be constructed.

More recent work on yellow fever has been carried on by Hideyo Noguchi who, between 1918 and 1924, isolated and cultivated the causative organism *Leptospira interrogans* and developed a preventive vaccine and curative serum for the disease.

But to Carlos J. Finlay goes the credit for pointing out the way along which these other workers have progressed.



El Mosquito Hipoteticamente Considerado como Agente de Trasmision de la Fiebre Amarilla

Anales de la Real Academia de Ciencias Médicas, Físicas y Naturales,
18: 147-169, 1881.

Señor Presidente.—Sres. Académicos:

Algunos años ha, en este mismo lugar tuve la honra de exponer el resultado de mis ensayos alcalimétricos, con los que creo haber demostrado definitivamente la excesiva alcalinidad que presenta la atmósfera de la Habana. Quizás recuerden algunos de los Académicos aquí presentes las relaciones conjeturales que creí poder señalar entre ese hecho y el desarrollo de la fiebre amarilla en Cuba. Pero de entónces acá mucho se ha trabajado, se han reunido datos más exactos y la etiología de la fiebre amarilla ha podido ser estudiada más metódicamente que en épocas anteriores. De ahí el que yo me haya convencido de que precisamente ha de ser insostenible cualquiera teoría que atribuya (p. 148) 'el origen ó la propagacion de esa enfermedad á influencias atmosféricas, miasmáticas, meteorológicas, ni tampoco al desaseo ni al descuido de medidas higiénicas generales. He debido pues abandonar mis primitivas creencias; y al manifestarlo aquí, he querido en cierto modo justificar ese cambio en mis opiniones, sometiendo á la apreciacion de mis distinguidos colegas una nueva serie de es-

tudios experimentales que he emprendido con el fin de descubrir el modo de propagarse la fiebre amarilla.

Debo advertir, empero, que el asunto de este trabajo nada tiene que ver con la naturaleza ó la forma en que puede existir la causa morbígena de la fiebre amarilla: me limito á admitir la existencia de una causa material transportable, que podrá ser un *virus* amorfo, un gérmen animal ó vegetal, una bacteria etc., pero que constituye, en todo caso, un algo tangible que ha de comunicarse del enfermo al hombre sano para que la enfermedad se propague. Lo que me propongo estudiar es el *medio* por el cual la materia morbígena de la fiebre amarilla se desprende del cuerpo del enfermo y se implanta en el hombre sano. La necesidad de admitir una intervencion extraña á la enfermedad para que ésta se transmita, resulta de numerosas consideraciones, algunas de ellas formuladas ya por Rush y Humboldt, á principios del siglo, y confirmadas luégo por observaciones más recientes. La fiebre amarilla unas veces atraviesa el Océano para ir á propagarse á ciudades muy distantes y de condiciones meteorológicas muy diferentes de las del foco de donde ha provenido la infeccion; miéntras que en otras ocasiones la misma enfermedad deja de transmitirse fuera de una zona epidémica estrecha, por más que la meteorología y la topografía de los lugares circunvecinos no revelen diferencias que expliquen ese comportamiento tan diverso de la misma enfermedad en dos localidades, al parecer, iguales. Admitida la ingerencia necesaria de un agente de trasmision que explicara las anomalías señaladas, es claro que sobre ese agente habría de recaer la influencia de todas las condiciones hasta ahora reconocidas como esenciales para que la fiebre amarilla (p. 149) se propague. No era, pues, posible buscar ese agente entre los microzoarios ni los zoófitos, porque en esas categorías ínfimas de la naturaleza animada, poco ó nada influyen las variaciones meteorológicas que más suelen afectar el desarrollo de la fiebre amarilla. Para llenar esta primera condicion fué preciso ascender hasta la clase de los insectos, y, teniendo en cuenta que la fiebre amarilla está caracterizada clínica, y tambien, segun trabajos recientes, histológicamente, por lesiones vasculares y alteraciones fisico-químicas de la sangre, parecía natural buscar el insecto

que hubiera de llevar las partículas infectantes del enfermo al hombre sano entre aquellos que penetran hasta el interior de los vasos sanguíneos para chupar la sangre humana. En fin, en virtud de consideraciones que fuera ocioso referir, llegué á preguntarme si no sería el mosquito el que trasmite la fiebre amarilla.

Tal fué la hipótesis que motivó la serie de estudios experimentales que voy á exponer.

La aplicacion de las ciencias auxiliares á la Medicina suele exigir conocimientos tan variados y tan especiales en los distintos ramos del saber humano, que no debemos extrañar la tardanza que los estudios realizados en tal ó cual provincia científica suelen experimentar ántes de poderse aprovechar en beneficio de nuestras investigaciones médicas. Nótase particularmente esa dificultad con respecto á la Historia Natural, porque las más de sus adquisiciones, fundadas en la observacion directa de fenómenos naturales, para que podamos utilizarlas, casi siempre requieren una completa revision desde el nuevo punto de vista que su aplicacion á las ciencias médicas implica. Sólo así se comprende el que más de un siglo despues que el ilustre Reaumur escribiera su admirable memoria sobre los hábitos del Mosquito, justamente considerada como un modelo de exacta é inteligente observacion y que, bajo un punto de vista general, parece casi agotar el asunto de que trata, cuando, ahora seis meses, yo recurrí á tan valiosa fuente, en busca de datos que me facilitasen el estudio que me habia propuesto, no hallé los que más falta me hacian (p. 150) y me fué preciso, no tan sólo emprender una comprobacion radical de los datos presentados por Reaumur, para cerciorarme de que eran tambien aplicables á los mosquitos de Cuba, sino tambien escudriñar otros pormenores que á Reaumur y á los demás naturalistas no les interesaba observar.

Comencemos por recordar á grandes rasgos la distribucion geográfica del mosquito. En términos generales puede decirse que en todas partes los hay, ménos en las cumbres elevadas. En efecto, el díptero que nos ocupa, el género *Culex*, que muchos creen especial tormento de las regiones tropicales, existe, por lo contrario, en todas las latitudes. En las regiones polares, los Lapones al par de los habitantes de las regiones equinocciales de

América, no pueden tomar el alimento ni acostarse á dormir en sus chozas, sino sumergidos en una atmósfera de humo, para librarse de esa plaga. Al aire libre los mosquitos se les meten por la boca y las narices; y esos hombres, á pesar de su cutis endurecido por el frio de sus inviernos, á duras penas logran preservarse por medio de velos saturados de grasas fétidas y untándose el cuerpo con crema ó manteca. En el Canadá, en Rusia, en Inglaterra, en Francia, en España, en toda Europa, en Siberia, en China, en los Estados Unidos, en la América del Norte, como en la del Sur, pululan los mosquitos. En el centro de Africa un viajero aleman, el Dr. Schweinfurst, fué atormentado por unos mosquitos de patas pintadas (spotty legged) cuya descripcion pudiera convenir al *C. mosquito* de Cuba y tambien al que el Dr. Arnold observó en Batavia, segun refiere Kirby, considerándolo como una especie no descrita, parecida al *C. annulatus*, pero sin pintas en las alas.

Nótase sin embargo en la misma distribucion geográfica alguna preferencia del mosquito á extenderse en los continentes ántes que en las islas, confirmandose así la observacion de Humboldt de que ese díptero es más abundante en las riberas de los grandes rios que no en los islotes que se encuentran en los mismos, y que se siente ménos el tormento de los mosquitos en el centro del rio que cerca de las riberas. Quizá á esto se (p. 151) deba al que los primeros historiadores del descubrimiento de la América no hagan especial mencion del mosquito en las Islas, durante los primeros viajes de Colon; pues no he encontrado mencion especial de ellos en las Antillas ántes de 1538, á propósito de una excursion de Hernando de Soto, cuyos soldados al atravesar un rio, cerca de Puerto de los Príncipes, fueron picados de tal manera por los mosquitos que tenian en las espaldas grandes manchas de sangre. A la misma inmunidad relativa de las islas débese sin duda atribuir el hecho siguiente que un viajero americano refirió al entomólogo Osten Sacker, [citado por el Dr. Taschenberg, Brehm IX, pág. 446]. Por el año de 1823 no se conocían aún los mosquitos en las islas de Hawai; mas entre los de 1828 á 1830, un buque viejo venido de Méjico fué abandonado en las costas de una de ellas. Pronto observaron los habitantes que al rededor

de ese lugar aparecian unos insectos desconocidos, chupadores de sangre. Esto despertó la atencion de los indígenas y algunos curiosos solían venir por las tardes á dejarse picar por esos insectos tan extraordinarios. Luégo se propagaron los mosquitos en esas islas y llegaron á ser una verdadera plaga.

Es cierto que el mosquito en todas las latitudes existe, mas no en todas las localidades se encuentra en igual abundancia. Alej. Humboldt y Bonpland, en sus viajes á la América equinoccial, dicen: "El tormento de los mosquitos y de los zancudos no es tan general bajo la zona tórrida como se cree generalmente. En las mesetas elevadas más de 400 toesas sobre el nivel del Océano, en las muy secas llanuras distantes de los grandes rios, por ejemplo, Cumaná y Calabozo, no hay sensiblemente más maringuinos que en la parte más habitada de Europa." La influencia de la sequedad y distancia de los rios, señalada por esos viajeros, desde luégo se comprende, toda vez que la larva del mosquito y su ninfa son acuáticas, y que, para propagarse, el insecto adulto tiene que depositar sus huevos en el agua. En cuanto al impedimento que las alturas oponen á su propagacion, estimo que será consecuencia de la misma dificultad que esos dípteros siempre experimentan en el vuelo ascendente (p. 152) despues de haberse llenado de sangre, máxime si se trata de especies como la del C. mosquito, cuyas alas son tan pequeñas, puesto que esa dificultad no podrá ménos que aumentar por efecto de la rarefaccion del aire en las alturas considerables. En tal caso, se comprende que el mosquito se aparte instintivamente de esos lugares. Tam bien refieren los viajeros ántes citados que el buen misionero Bernardo Zea se habia construido una habitacion sobre un tablado de troncos de palma, donde ellos iban por las noches á secar las plantas que habian recogido y á redactar su Diario. "El misionero habia observado con razon, dicen, que los insectos abundan comunmente en la capa más baja de la atmósfera, que se acerca de la tierra hasta unos 12 ó 15 piés de altura." Más adelante agregan esos autores: "á medida que se sube hácia la llanura ó meseta de los Andes, estos insectos desaparecen y allí se respira un aire puro . . . á doscientas toesas de altura ya no se temen los zancudos ó musticos."

Históricamente el mosquito es uno de los insectos más antiguamente observados. Aristóteles y Plinio hacen referencia á su trompa, que sirve á la vez para horadar la piel y chupar la sangre. El historiador griego Pausanias [citado por Taschenberg] menciona la ciudad de Myus, en Asia menor, situada en una ensenada cuya comunicacion con el mar vino á cerrarse luégo; cuando el agua del lago que así se formara dejó de ser salada, resultó tal plaga de mosquitos, que los habitantes abandonaron la ciudad y se trasladaron á Mileto. Así tambien, leemos en las Décadas de Herrera, Juan de Grijalva, cuando por primera vez descubrió las costas de Nueva España, el año de 1518, hubo de ocupar con su gente la isleta que nombró San Juan de Ulúa, teniendo que hacer sus chozas “encima de los más altos medanos de arena de la isleta, por huir de la importunidad de los mosquitos.” De allí mismo tuvo luégo que salir al cabo de siete dias, “no se pudiendo valer de los mosquitos,” y Bernal Díaz del Castillo tuvo que irse á unos adoratorios de los indios, “huyendo de la molestia de los mosquitos.” En fin, en 1519, casi en el mismo (p. 153) sitio donde hoy se levanta la moderna Veracruz “los mosquitos zancudos, dice Herrera, y los chicos que son peores, fatigaban la gente de Cortés.”

Dos especies de mosquitos he observado en la Habana desde el mes de Diciembre próximo pasado que vengo estudiando esos insectos. Una es grande, de color amarillo, con patas largas y delgadas, sin pintas notables; supongo que sea el idéntico zancudo que fatigaba la gente de Cortés en los arenales de San Juan de Ulúa por el año de 1519, y el *Culex cubensis* descrito en la obra de La Sagra. Su cuerpo, medido desde la raíz de la trompa hasta la extremidad anal, tiene de 5 á 7 milímetros de longitud. Esta especie sale exclusivamente de noche, despues de las nueve ó diez, y prosigue sus molestas evoluciones hasta la madrugada: á ella han pertenecido casi todos los mosquitos que he encontrado en los mosquiteros, donde una vez que se han llenado de sangre, suelen permanecer parte del dia, miéntras digieren la sangre que han chupado. La otra especie es el *Culex Mosquito*, que nuestro distinguido naturalista cubano, D. Felipe Poey, llevó á París en los años 1817 ó 1820, donde fué clasificado por M.

Robineau Desvoidy. He observado dos variedades de esta especie: una, la mayor, esbelta y vigorosa, de color gris oscuro, mide poco ménos que el zancudo; y otra, más pequeña, de cuatro á cuatro y medio milímetros de longitud. No me he ocupado en buscar caracteres diferenciales entre estas dos variedades de una misma especie, puesto que la diferencia de sus dimensiones bastaba para mi objeto actual. Ambas variedades del *C. mosquito* presentan los distintivos siguientes: su cuerpo es oscuro, á veces casi negro ó color de acero; la superficie ventral y la superior del abdómen están como reforzadas por una capa espesa anillada de blanco, predominando á veces la parte blanca, de manera que parecen blanco ó blanquecino el fondo y oscuros los anillos. En cada lado del abdómen se ven dos hileras de seis puntos anacardados, entre los cuales se coloca la membrana transparente que ha de distenderse para dejar ver la sangre ú otro líquido que el insecto ingiera. Hay cinco (p. 154) anillos blancos muy característicos en las patas traseras; corresponden á las articulaciones del tarso, metatarso y de la tibia, donde á veces existe otra, sexta, mancha blanca. En las patas del medio y en las delanteras hay dos ó tres pintas blancas. En los lados del tórax hay ocho ó diez puntos blancos redondos, y en la parte antero-superior del mismo tórax se vé un conjunto de líneas blancas que figura bastante bien una lira de dos cuerdas, trazada en blanco sobre fondo negro. Los palpos y las antenas tambien llevan pintas blancas. Algunas de esas pintas con el tiempo y el roce suelen borrarse, pero es raro que dejen de persistir las más características. Las alas del *C. mosquito*, cuya nervadura excuso describir aquí, no presentan las manchas señaladas en el *Culex annulatus* de Europa, y son tan cortas que cerradas dejan descubierto el último segmento del cuerpo. Parece inútil advertir que, para observar los caracteres que dejo señalados, es indispensable emplear un vidrio de aumento; las lentes aplanáticas, de dos y media á tres pulgadas de foco, me han parecido las más convenientes.

El macho de ambas especies se reconoce fácilmente por sus antenas plumosas, que le dan el aspecto de llevar bigote, y por su trompa que parece trífida, debido á que los palpos son tan largos como ella, y despues de quedar aplicados contra ella en

los dos tercios superiores, se separan ántes de llegar á la punta, contrastando notablemente con la trompa lisa de la hembra, cuyos palpos no llegan sino á una sexta parte de su longitud.

Las dos especies de mosquito no salen á las mismas horas: al zancudo corresponde la noche y al *C. mosquito* el dia. Deseoso de averiguar el motivo de ese reparto del dia y de la noche entre las dos especies, pensé que el zancudo, á pesar de sus dimensiones mayores y su aspecto más robusto, quizá no estuviese organizado para resistir el calor del sol de nuestro verano, mientras que el mosquito con su integumento reforzado podría resistirlo mejor. Hice, pues, el siguiente experimento: el 9 de Junio, á las 12 del dia, expuse á los rayos directos del sol los dos termómetros de mi sicrómetro; al (p. 155) cabo de media hora el seco marcaba $42^{\circ} 25$ y el húmedo $31^{\circ} 75$; coloqué entónces, en lugar del instrumento, un tubo donde estaba aprisionado un zancudo, cogido ya desde cinco dias, pero vivo y ágil todavía,—á los cinco minutos estaba muerto. Puse entónces otro tubo igual con un *Culex* mosquito, y despues de dejarlo quince minutos lo encontré sin daño alguno, y siguió vivo durante veinte y cuatro horas más dentro de su tubo.

Sabido es que sola la hembra del mosquito es la que pica y chupa la sangre, mientras que el macho se sustenta con jugos vegetales, principalmente los dulces; pero hasta ahora no he visto señalado en los autores que han escrito sobre el asunto la circunstancia de que tampoco la hembra pica ántes de haber sido fecundada por el macho. Esto, al ménos, es lo que parece deducirse de los experimentos siguientes:

Una hembra del *C. mosquito*, cogida al salir de la ninfa y conservada dos y tres dias viva, en todo ese tiempo no se la puede hacer picar. Varias veces he repetido este experimento y siempre el resultado ha sido negativo.

Las hembras aprisionadas en el acto de la fecundacion, al separarse del macho pican en seguida y se llenan de sangre.

En fin, casi todas las hembras cogidas despues de haberse saciado de sangre, al cabo de algunos dias ponen huevos, mientras que las fecundadas que no llegan á chupar la sangre mueren sin poner.

No es, por consiguiente, para su propio sustento que la hembra del mosquito se muestra ávida de sangre viva; y, en efecto, no se concebiría cómo, para sustentar un cuerpo tan diminuto, habría de necesitarse cantidad tan enorme de un alimento tan rico como la sangre pura. Era, pues, forzoso admitir que la sangre ingerida estaría destinada á otros fines, relacionados con la propagacion de la especie. Me inclino á suponer, como la más natural de mis hipótesis, que la influencia de la sangre es debida á su temperatura; porque así se comprende que si la maduracion de los óvulos contenidos en los ovarios del mosquito hembra requiriese una temperatura de (p. 156) 37°C. , ésta, en las condiciones meteorológicas de nuestra Isla, difícilmente podría obtenerse con tanta seguridad y certeza como por el medio empleado por el mosquito, ingiriendo un volúmen de sangre considerable de la temperatura necesaria, y, quizá, alguna vez convenga al mosquito elegir para sus fines algun febricitante cuya sangre de 39° á 40° active más aún el momento de la ovacion. Así tambien se comprende por qué el zancudo y otros mosquitos grandes pueden absorber en una sola vez toda la sangre necesaria para madurar con su calor todos los 200 á 350 huevos que han de poner y efectivamente ponen en una sola postura; mientras que las especies más pequeñas, como el *C. mosquito*, necesitan llenarse varias veces de sangre para empezar á poner y, por lo regular, hacen la ovacion en dos ó tres sesiones.

Una vez que el mosquito hembra se ha saciado de sangre emplea dos, tres y hasta cuatro días, segun las especies, en digerirla; durante cuyo tiempo, escondida de las miradas indiscretas, se pasa horas enteras en unas operaciones curiosas que Reaumur no supo explicarse, porque sólo las observó en el estado de libertad. Aprisionadas en tubos de vidrio, es fácil cerciorarse de que esos movimientos consisten en embarrarse todo el cuerpo con una secrecion viscosa que el mosquito recoge de la extremidad del ano con sus patas traseras y se unta con ellas todo el cuerpo: cada pata por separado, el abdómen, las alas, el tórax, la cabeza y hasta la misma trompa. Como me ha sugerido nuestro distinguido académico, *facile princeps* entre los naturalistas cubanos, D. Felipe Poey, esta operacion es probable que tenga por objeto

hacer impermeable á la hembra del mosquito para cuando vaya á poner sus huevos sobre el agua. Tambien durante la digestion de la sangre ingerida depone el mosquito partículas sanguinolentas, que tienen la facultad de disolverse con extraordinaria facilidad en el agua, áun despues de haber permanecido secas durante varios meses. Esto se debe sin duda á la combinacion de la sangre con la saliva que el insecto vierte en la herida, destinada segun opinion general, á dar mayor fluidez á la sangre que está (p. 157) chupando. Por lo regular, despues de haber ingerido toda la sangre que corresponde á una picada no interrumpida, el mosquito no vuelve á picar, ántes al contrario, evita posarse sobre la piel desnuda (sin duda porque le desagrada entónces el calor), hasta haber digerido toda la sangre. Este es el momento de la aovacion en el zancudo.

No repetiré la descripcion ya clásica de Reaumur, en que tan gráficamente explica el modo cómo la hembra del mosquito de Europa forma su botecillo tan elegante de huevos y lo echa al agua. Parece ser la misma operacion la que ejecuta el zancudo de Cuba. Pero habiendo observado que las hembras zancudas, despues de poner su botecillo de huevos, suelen quedar muertas sobre el agua, he llegado á creer que los cadáveres que Reaumur solía considerar como tantas recién nacidas naufragadas al desprenderse de la ninfa, en realidad serían los de las madres que se dejan morir al lado de sus huevos, quizá para contribuir á la alimentacion futura de las larvas.

Las tres operaciones sucesivas: fecundacion, picada y aovacion ó postura de huevos, constituyen un ciclo ineludible dentro del cual habrá de girarse la existencia del mosquito. La primera de estas funciones, la fecundacion, es probable que, como en los demás insectos, tenga lugar una sola vez, bastando una sola impregnacion del saco seminal por el sémen del macho, para que en lo sucesivo queden fecundados todos los huevos que atraviesen la parte correspondiente de los oviductos. En la abeja cubana, ya nos lo ha dicho D. Felipe Poey, basta una sola fecundacion de la hembra por el macho para que resulten fecundados todos los huevos que á millares debe poner aquella, durante los dos ó tres años que durará su existencia. Con las hembras del

género *Culex* hasta ahora estudiadas, no hay lugar de poner á prueba esa fecundacion prolongada, puesto que la aovacion se efectúa en ellas en una sola vez; pero no sucede así con las hembras del *C. mosquito*. Estas ponen sus huevos aislados ó en hileras de nueve á quince, separados ó juntos, unas veces sobre el agua, otras sobre los cuerpos adyacentes bastante cerca del nivel para que una (p. 158) pequeña elevacion permita al agua bañarlos. Cualquiera que sea el valor de la hipótesis que he propuesto, para explicar la necesidad que tiene el *C. mosquito* de picar varias veces y llenarse otras tantas de sangre viva, á fin de llevar á cabo la postura de todos sus huevos, lo cierto es que las hembras de esa especie siempre se hallan en disposicion de volver á picar despues que han digerido la sangre que habían chupado en la primera picada. En el caso de una de esas hembras cogida en el mes de Enero del corriente año, ella picó doce veces y tres veces efectuó la aovacion durante los 31 dias que vivió; habiendo ido á morir en los Estados Unidos, donde á la sazón la temperatura exterior estaba por debajo de 0°C.

Con el *C. cubensis* ó el zancudo, por lo contrario, no he logrado nunca una segunda picada con las hembras aprisionadas, hubiesen ó no puesto sus huevos. Posible es, sin embargo, que, en estado de libertad, ellas necesiten á veces varias picadas sucesivas ántes de proceder á la aovacion; sí he observado alguna vez que venian á picarme, teniendo ya el vientre ocupado por alguna sangre; pero he creido que esto resultara por haber sido interrumpida la picada anterior ántes que el insecto hubiese ingerido toda la sangre que le correspondiera.

Es evidente que bajo el punto de vista en que estoy considerando el mosquito, la especie *C. mosquito* se encuentra en condiciones admirables de aptitud para llevar de un individuo á otro una enfermedad que fuese transmisible por medio de la sangre, toda vez que tiene múltiples ocasiones de chupar sangre de distintas procedencias y tambien de inficionar á distintos individuos; aumentando notablemente las probabilidades de que su picada pueda reunir las coincidencias necesarias para que se realice la trasmision. Por otro lado, el *C. cubensis*, al absorber por su trompa mayor cantidad de sangre virulenta, deberá

quedar más impregnada y en condicion de producir una inoculacion más grave, máxime si ésta se efectúa á los pocos instantes de haber salido las lancetas de la zancuda del vaso capilar de un enfermo, como habrá de suceder cuando su primera picada ha sido interrumpida. Aquí, pues, (p. 159) será más grave la infeccion, pero ménos probable su ocurrencia.

No es posible, empero, comprender las extraordinarias facilidades que la picada del mosquito ofrece para la inoculacion de cualesquiera particular contagiosas que la sangre pudiese contener, sin ántes hacerse cargo de la conformacion y estructura del aparato que la hembra del mosquito emplea para picar y chupar la sangre. Lo que se vé de la trompa del mosquito en condiciones normales es la vaina, resultado de la transformacion del labio inferior: ella nace por un pedículo implantado en la base de la cabeza, debajo de las otras piezas orales, está hendida en su parte superior y en toda su longitud hasta llegar á un botoncito terminal, que considero análogo á un par de palpos labiales, y de cuya extremidad salen las puntas de las otras piezas que contiene. La vaina del *C. mosquito*, á cuya especie he limitado mis observaciones, mide dos y medio milímetros de largo; una línea francesa, dice Reaumur que tenía la trompa de la especie que el observó: y como quiera que nuestro mosquito á veces mete sus lancetas hasta muy cerca de su insercion, se verá cuan fácilmente habrá de alcanzar cualquier vaso que se encuentre á ménos de un quinto de centímetro de la superficie cutánea. Dentro de la vaina existen dos tubos que parecen sueltos en el fondo de su concavidad, donde los he visto algo tortuosos; los dos se reunen en un tronco comun, el cual ocupa la concavidad del pedículo de la vaina. Creo que por esos tubos vierta el mosquito la saliva acre é irritante que ocasiona el escozor de la picada, y destinada, segun creen los naturalistas, á hacer más fluida la sangre que ha de correr por el sifon. En el interior de la vaina se encuentran cinco piezas: una, la principal, es ímpar, procedente del labro ó labio superior, de consistencia córnea y prolongada en forma de espolon hondamente acanalado y abierto por su parte superior, en toda su longitud, hasta terminar en una punta como la de un

limpia-dientes que se hiciese cortado en un cañon de pluma largo y angosto. Esta pieza es rígida y en toda su superficie externa presenta un labrado (p. 160) muy curioso, como si sobre ella estuviese aplicada una red cuyas mallas, en relieve, formáran unos paralelógramos pequeños con los ángulos más agudos dirigidos en el sentido longitudinal. Dentro de esas mallas innumerables fácilmente podrían alojarse partículas de la sangre chupada. Las otras cuatro piezas consisten en dos pares de lancetas flexibles, correspondientes á las dos mandíbulas y á las maxilas é implantadas á la raíz de los dos palpos maxilares que se ven de cada lado de la trompa. La estructura de estas dos clases de lancetas es enteramente distinta: la lanceta mandibular consiste en una pieza acanalada y con tendencia á conservar su forma encorvada; su cara externa es convexa y presenta en toda su extension unas crestas transversales, paralelas y compuestas, segun creo, de unos dientes. Tambien los bordes de su hendidura longitudinal presentan unos dientes de filo muy acerado; la punta de esta lanceta es encorvada y convexa, presentando dientes en sus bordes libres hasta la misma extremidad, cuya sutileza y fuerza deben ser muy considerables, á juzgar por su aspecto. Las lancetas maxilares, cuyo origen se encuentra más abajo del de las mandibulares, tienen la forma de una cinta cuyos bordes estuvieran doblados hácia adentro, como un dobladillo, y cuyo borde libre, así doblado, estuviese armado de una franja de dientes muy finos y largos: esta lanceta, en su conjunto, se asemeja á las hojas largas y angostas de ciertas yerbas, y tambien por su punta ancha, de doble filo, reforzada en el medio por una nervura longitudinal. Todas estas piezas se amoldan sobre el espolon del labro de tal manera, que al separar la vaina, ántes de la disociacion de las lancetas, parece imposible que la varilla redonda ú ovalada con su punta única, aguda y afilada que se tiene á la vista pueda ser el conjunto de las cinco piezas que acabo de describir.

La operacion de la picada comienza por la exploracion que hace el mosquito, tentando la piel con la punta de su trompa hasta encontrar un lugar conveniente y entónces se planta con decision sobre sus seis patas (á veces mantiene las dos traseras (p. 161)

levantadas), el tórax fuertemente inclinado hacia abajo, la cabeza y la trompa casi verticales. En seguida, con la simple vista ó mejor con un vidrio de aumento, se ve la vaina encorvarse hacia atras, en su parte superior, y gradualmente doblarse en forma de una < horizontal, cuyas ramas van gradualmente aproximándose á medida que las lancetas penetran en la piel. Estas aparecen en forma de un alambre muy sutil tendido entre las extremidades de la < figurada por la vaina y se las vé moverse al par que los palpos maxilares, hasta que, habiendo penetrado en la luz de algun vaso capilar, el insecto se inmoviliza miéntras se llena, al parecer sin ningun esfuerzo de su parte, con la sangre roja y caliente de su víctima. Durante esta operacion se siente á veces un escozor instantáneo, debido á la saliva que el mosquito vierte en la herida por la extremidad de la vaina, cuyo boton se halla cogido en la cisura. El vientre se abulta y la sangre se hace visible al través de sus paredes laterales transparentes. Esta operacion por lo regular dura varios minutos y yo la he visto prolongarse hasta siete.

Sabido es que los mosquitos, aunque nunca desaparecen del todo en la Habana, tienen sin embargo épocas estacionales en que son mucho más numerosos que en otras. Su número me ha parecido aumentar progresivamente desde Abril ó Mayo hasta Agosto, para de allí decrecer gradualmente hasta Febrero y Marzo. Pero hay un punto relativo al estudio que venimos haciendo, que no es posible desatender por razon de las numerosas aplicaciones que puede tener en ciertos casos, hasta ahora inexplicados, de reproduccion de epidemias de fiebre amarilla, sin nueva importacion, en localidades hasta entónces consideradas inmunes. Me refiero á la hibernacion del mosquito, fenómeno que no se observa en nuestro clima, al ménos en todas sus fases, pero que constituye, segun las más autorizadas opiniones, el modo regular de propagarse la especie en los climas frios. Dice en efecto el Dr. Taschenberg: "las hembras fecundadas de la última generacion hibernan en los más diversos escondrijos, principalmente en las cuevas de las (p. 162) casas, para luégo propagar su especie en la siguiente primavera."

Eu cuanto á las condiciones que favorecen el desarrollo de los

mosquitos citaré el calor, la humedad, la presencia de aguas estancadas, las localidades bajas y oscuras, la ausencia de viento y la estacion del verano; pero no estará de más recordar la observacion de Humboldt, de que la abundancia de los mosquitos no siempre obedece á condiciones meteorológicas ni topográficas determinables.

He hablado ya de la dificultad que el mosquito, por motivo de sus alas relativamente pequeñas, necesariamente ha de experimentar para elevarse en el aire despues de haberse saciado de sangre. La misma causa impedirá tambien que el mosquito se aparte mucho del lugar donde haya efectuado su última picada y, en general, que pueda mantenerse mucho tiempo en el aire, ni trasladarse á distancias considerables, sin posarse. Mas esto no se opone á que, escondido entre la ropa, en un sombrero, en una maleta de viaje, etc., el mosquito, despues de una picada reciente, pueda ser trasportado á grandes distancias llevando quizá, en sus lancetas, el gérmen inoculable de la enfermedad.

En fin, débese tener en cuenta las preferencias que los mosquitos manifiestan hácia ciertas razas é individuos, notándose que la ménos atormentada parece ser la africana, y los individuos más perseguidos por ellos los de razas del norte recién venidos á las regiones tropicales de América. Parece verosímil que esto obedezca al grado de espesor de la piel y á las condiciones en que se efectúa la circulacion capilar cutánea, puesto que esas circunstancias han de influir en la facilidad con que el mosquito hembra podrá procurarse la sangre que necesita para completar el ciclo de su existencia.

Hecha esta larga, pero necesaria explicacion de los hábitos de nuestros mosquitos de Cuba y del C. mosquito en particular, veamos ¿de qué medios podría valerse el mosquito para comunicar la fiebre amarilla, si esta enfermedad fuese realmente transmisible por la inoculacion de la sangre? Lo más (p. 163) natural, al hacernos esta pregunta, es pensar en la sangre virulenta que el mosquito ha chupado á un enfermo de fiebre amarilla y que puede ascender á cinco y hasta 7 ú 8 milímetros cúbicos, los mismos que, si el mosquito muriese ántes de haberlos digerido, quedarían en excelentes condiciones para conservar durante largo

tiempo sus propiedades infectantes. También podrá pensarse, sin duda, en la misma sangre que, en forma de excremento, depositan los mosquitos en las aguas potables y otras, y que bien pudiera llevar la infección si ésta fuese susceptible de introducirse por la boca. Pero los experimentos de Ffirth y ciertas consideraciones directamente enlazadas con mi modo de apreciar la patogenia de la fiebre amarilla no me permitían detenerme en ninguno de esos modos de propagación. Voy á decir por qué. Cuando la Comision Norte Americana de Fiebre Amarilla al despedirse de nosotros, ahora dos años, nos dejó su valiosa colección de fotografías de las preparaciones microscópicas hechas por nuestro socio corresponsal el Dr. Sternberg, lo que más llamó mi atención fué la circunstancia allí demostrada de que los glóbulos rojos de la sangre salen enteros en las hemorragias de la fiebre amarilla; y como quiera que esas hemorragias se efectúan á veces sin rotura perceptible de los vasos, era forzosa la deducción de que, siendo ese síntoma el carácter clínico más esencial de la enfermedad, habría que buscarse la lesión principal en el endotelio vascular. Pensando luego en las circunstancias de que la fiebre amarilla es transmisible, que no ataca sino una vez á un mismo individuo, y que siempre presenta, en sus manifestaciones, un orden regular como el de las fiebres eruptivas, llegué á formarme una hipótesis en la que consideraba esa enfermedad como una fiebre eruptiva cuya erupción se hiciese en el endotelio vascular. El primer período sería el de la fiebre de invasión, la remisión coincidiría con el período de erupción, y el tercer período sería el de descamación. Si ésta se efectúa en buenas condiciones, el enfermo sólo presentará los indicios de una filtración exagerada de algunos elementos de la sangre al través del endotelio nuevo: (p. 164) si en malas el endotelio, mal repuesto, no podrá impedir la salida de los elementos figurados de la sangre, vendrán las hemorragias pasivas y habrá peligro inminente para el paciente. En fin, asimilando esta enfermedad á la viruela y á la vacuna, me dije que para inocularla habría que ir á buscar la materia inoculable en el interior de los vasos de un enfermo de fiebre amarilla y llevarla también al interior de un vaso sanguíneo de otro individuo en aptitud de recibir la inoculación. Condiciones todas,

que el mosquito realiza admirablemente con su picada y que sería punto ménos que imposible á nuestras manos imitar, con los instrumentos comparativamente toscos y groseros que puede producir el más hábil de nuestros artesanos.

Tres condiciones seran pues necesarias para que la fiebre amarilla se propague: 1. Existencia de un enfermo de fiebre amarilla, en cuyos capilares el mosquito pueda clavar sus lancetas é impregnarlas de partículas virulentas, en el período adecuado de la enfermedad; 2. Prolongacion de la vida del mosquito entre la picada hecha en el enfermo y la que deba reproducir la enfermedad; y 3. Coincidencia de que sea un sujeto apto para contraer la enfermedad alguno de los que el mismo mosquito vaya á picar despues.

La primera de estas condiciones, desde que el Dr. D. Ambrosio G. del Valle ha comenzado á publicar sus valiosas tablas mortuorias, puede asegurarse que jamás ha dejado de hallarse realizada en la Habana; en cuanto á la 2ª. y la 3ª., es evidente que las probabilidades de que resulten cumplidas dependerán de la abundancia de los mosquitos y del número de individuos susceptibles de recibir la inoculacion que se encuentren en la localidad. Creo que, efectivamente, en la Habana han coincidido siempre las tres condiciones señaladas los años en que la fiebre amarilla ha hecho sus mayores estragos.

Tal es mi teoría, señores, y en verdad ella ha venido á robustecerse singularmente con las numerosas coincidencias históricas, geográficas, etnológicas y meteorológicas que ocurren entre los datos que se refieren al mosquito y los que tenemos (p. 165) acerca de la fiebre amarilla, y tambien con la circunstancia de que podemos con su auxilio explicar circunstancias hasta ahora inexplicables por las teorías existentes. La fiebre amarilla no fué conocida en la raza blanca hasta despues del descubrimiento de América, y segun Humboldt es opinion tradicional en Veracruz, que allí ha existido esa enfermedad desde que vinieron á sus playas los primeros exploradores españoles. Allí tambien hemos visto que los españoles desde su primera venida señalaron la presencia de mosquitos, y, con más insistencia que en ningun otro lugar de América, en los mismos arenales de San Juan de

Ulúa. Las razas más expuestas á padecer la fiebre amarilla son tambien las que más sufren de las picadas de los mosquitos. Las condiciones meteorológicas que más favorecen el desarrollo de esa fiebre son las mismas que acrecientan el número de los mosquitos: en abono de cuyo aserto puedo citar varias epidemias parciales respecto de las cuales se afirma, bajo la garantía de médicos competentes, que durante la prevalencia de la fiebre amarilla los mosquitos habian sido mucho más numerosos que en épocas pasadas, haciéndose constar, en un caso, que los mosquitos eran de especie distinta de las que allí solían observarse, y que llevaban unas manchas grises en el cuerpo. Respecto á la topografía de la fiebre amarilla, el mismo Humboldt, que señala las alturas hasta donde suelen llegar los mosquitos, en otro lugar menciona los límites de elevacion hasta donde suele propagarse la fiebre amarilla. En fin, en el caso muy notorio del vapor de los Estados Unidos "Plymouth," en que 2 casos de fiebre amarilla se desarrollaron en alta mar despues de haber sido desinfectado y congelado el buque durante todo el invierno, y de haber transcurrido cuatro meses desde el último caso observado abordo, en el mes de Noviembre anterior, se explica perfectamente por la hibernacion de aquellos mosquitos que hubiesen picado á los anteriores casos de vómito y luégo, encontrándose otra vez bajo una temperatura tropical, volvieron á salir de su letargo y picaron á dos de los nuevos tripulantes del buque.

(p. 166) Apoyado pues en esas razones, determiné someter á prueba experimental mi teoría, y despues de obtener las debidas autorizaciones, procedí de la manera siguiente.

El dia 28 de Junio próximo pasado, llevé á la casa de salud de Garcini un mosquito cogido ántes de que hubiera picado, y le hice picar y llenarse de sangre en el brazo de un enfermo, D. Camilo Anca, que se hallaba en el quinto dia de fiebre amarilla, perfectamente caracterizada, y de cuya enfermedad falleció dos dias despues. Habiendo luégo elegido á F. B., uno de los veinte individuos sanos no aclimatados á esa enfermedad, que se encuentran actualmente sometidos á mi observacion, le hice picar, el 30 de Junio, por el mismo mosquito. Teniendo entónces en cuenta que la incubacion de la fiebre amarilla, comprobada en algunos casos especiales, varía de uno á quince dias,—seguí ob-

servando al citado F. B.—El día 9 empezó á sentirse mal, y el 14 entró en el Hospital con una fiebre amarilla benigna, pero perfectamente caracterizada por el íctero y la presencia de albúmina en la orina, la cual persistió desde el tercero hasta el noveno día.

El día 16 de Julio hice picar en la misma casa de salud de Garcini un caso de fiebre amarilla grave, Don Domingo Rodriguez, en tercero ó cuarto día de enfermedad. El día 20 me hice picar á mí mismo por el mismo mosquito, y en fin, el 22, hice picar á A. L. C., otro de los veinte observados. A los cinco días entró en el hospital con fiebre, dolores fuertes de cabeza y de cintura é inyeccion de la cara; duraron tres días estos síntomas, entrando en convalescencia el individuo sin haber presentado íctero ni albuminuria. Fué diagnosticado de fiebre amarilla abortiva por el facultativo de asistencia.

El día 29 de Julio hice picar por un mosquito á D. L. R. que se hallaba gravemente atacado de fiebre amarilla en la casa de salud de Garcini en tercer día de la enfermedad. El 31 hice picar por el mismo mosquito á D. L. F., otro de los veinte individuos de mi observacion. El 5 de Agosto á las dos de la madrugada fué invadido de los síntomas de una fiebre (p. 167) amarilla ligera; presentó luégo algun íctero, pero creo que no llegó á presentar ninguna albúmina; en todo caso su esfermedad fué calificada de fiebre amarilla abortiva.

En fin, el 31 de Julio hice picar por otro mosquito al mismo D. L. R. enfermo de fiebre amarilla de la casa de salud de Garcini, en quinto día ya de la enfermedad, de la cual falleció al día siguiente. El 2 de Agosto hice picar por el mismo mosquito á D. G. B., otro de mis veinte observados. Hasta ahora esta última inoculacion no ha producido resultado; pero como quiera que no han transcurrido sino doce días, todavía se encuentra dentro de los límites de la incubation. (1)

(1) Este individuo, D. G. B., se presentó el día 17 de Agosto al reconocimiento, manifestando que desde unos 6 días venia padeciendo dolores de cabeza, inapetencia y malestar general. El 24 le encontré con alguna fiebre (Pulso 100; temperatura 38°2), y manifestó haber tenido fiebre más alta la víspera y el mismo día, por la mañana. No pasó, empero, de una fiebre muy ligera, puesto que el enfermo no tuvo que darse de baja, ni exigió medicacion alguna. Cesó la fiebre, pero los dolores de cabeza continuaron algunos días más.

Otro individuo, I. C., de los veinte, fué picado el día 15 de Agosto, por un mosquito que, dos días ántes se habia llenado en el brazo de un enfermo del Hospital Militar, en

Debo advertir que los individuos que acabo de citar son los únicos á quienes he inoculado por el mosquito, de la manera indicada, y que desde el 22 de Junio hasta ahora (en el término de siete semanas) no han ocurrido entre mis veinte observados más casos de fiebre amarilla confirmada, ni tampoco de forma abortiva, que los tres primeros inoculados.

Estas pruebas son ciertamente favorables á mi teoría, pero no quiero incurrir en la exageracion de considerar ya plenamente probado lo que aún no lo está, por más que sean ya muchas las probabilidades que puedo invocar en mi favor. Comprendo demasiado, que se necesita nada ménos que una demostracion irrefutable para que sea generalmente aceptada una teoría que discrepa tan esencialmente de las ideas hasta ahora propagadas acerca de la fiebre amarilla; mas, entretanto se proporcionan los datos de que aún carecemos, séame permitido (p. 168) resumir en las siguientes conclusiones los puntos más esenciales que he tratado de demostrar.

CONCLUSIONES.

1ª. Queda comprobado que el C. mosquito pica, por lo regular, varias veces en el curso de su existencia, no tan sólo cuando su primera picada ha sido accidentalmente interrumpida, sino tambien cuando ha podido saciarse por completo, transcurriendo, en este caso, dos ó más dias entre sus picadas.

2ª. Como quiera que la disposicion de las lancetas del mosquito se adaptan muy bien á retener partículas que se encuentren suspendidas en los líquidos que el insecto ingiere, no puede negarse la posibilidad de que un mosquito conserve en sus lancetas partículas del virus contenido en una sangre enferma y con el mismo inocule á las personas á quienes en lo sucesivo vaya á picar.

3ª. La experimentacion directa para determinar si el mosquito

5.º dia de fiebre amarilla. No parece que este inoculado haya estado formalmente enfermo hasta ahora (Setiembre 1.º). No he podido verle despues de la inoculacion, y sólo por aviso verbal tuve noticia de que se hallaba algo enfermo los dias 24 y 25 de Agosto, pero tampoco tuvo que darse de baja.

puede transmitir la fiebre amarilla de la manera indicada, se ha reducido á cinco tentativas de inoculacion, con una sola picada, y éstas dieron por resultado: un caso de fiebre amarilla benigna, pero perfectamente caracterizada con albuminuria é íctero; dos casos calificados de *fiebre amarilla abortiva* por los facultativos de asistencia; y dos de fiebres efímeras ligeras, sin carácter definido (1). De lo cual se infiere que la inoculacion por una sola picada no es suficiente para producir las formas graves de la fiebre amarilla, debiéndose aplazar el juicio respecto á la eficacia de la inoculacion para cuando sea posible experimentar en condiciones absolutamente decisivas, esto es, fuera de la zona epidémica.

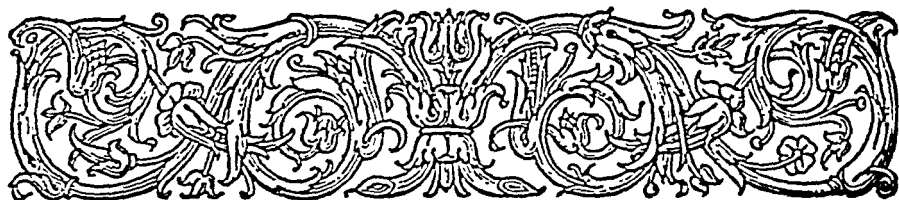
4ª. Si llegase á comprobarse que la inoculacion por el mosquito no tan sólo puede reproducir la fiebre amarilla, sino que es el medio general por el cual la enfermedad se propaga, las condiciones de existencia y de desarrollo de ese díptero explicarían las anomalías hasta ahora señaladas en la (p. 169) propagacion de la fiebre amarilla y tendríamos en nuestras manos los medios de evitar, por una parte, la extension de la enfermedad, mientras que, por otra, podrían preservarse con una inoculacion benigna los individuos que estuviesen en aptitud de padecerla.

Mi única pretension es que se tome nota de mis observaciones y que se deje á la experimentacion directa el cuidado de poner en evidencia lo que hay de cierto en mis conceptos. Esto no quiere decir, empero, que yo rehuya la discusion de las ideas que he emitido; ántes al contrario, tendré el mayor gusto en oír las advertencias ú objeciones que quisieren hacerme mis distinguidos compañeros.

Habana, 14 de Agosto de 1881.

Cárlos Finlay.

(1) Respecto de estos dos últimos, véase la nota anterior.



The Mosquito Hypothetically Considered as the Agent of Transmission of Yellow Fever

Read before the Royal Academy of Medical, Physical and Natural Sciences¹

Session of August 14th, 1881.

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Mr. President, Gentlemen:

SOME years ago I had the honor to submit to your consideration the results of my alkalimetric experiments, by which I think I have definitely demonstrated the excessive alkalinity which prevails in the atmosphere of Havana. Some of the Members now present, may perhaps remember the relations which I then attempted to establish between that peculiarity and the development of yellow fever in Cuba. Much however has been done since that time, more accurate data have been obtained, and the etiology of yellow fever has been more methodically studied. In consequence thereof I feel convinced that any theory which attributes the origin and propagation of yellow fever to atmospheric influences, to miasmatic or meteorological conditions, to filth or to the neglect of general hygienic precautions, must be considered as

¹ Translated by Dr. Finlay from the *Anales de la Academia de Ciencias Médicas, Físicas y Naturales de la Habana*, Vol. XVIII, p. 147. Vide also *Revista de la Asociación Médico-Farmacéutica de la Isla de Cuba*, January 1902, p. 273.

utterly indefensible. I have, therefore, been obliged to abandon my former ideas, and shall now endeavor to justify this change in my opinions, submitting to your appreciation a new series of experiments which I have undertaken for the purpose of discovering the manner in which yellow fever is propagated.

In this paper I shall not concern myself with the nature or form of the morbid cause of yellow fever, beyond postulating the existence of a material, transportable substance, which may be an amorphous virus, a vegetable or animal germ, a bacterium, etc., but, at any rate, constitutes something tangible which requires to be conveyed from the sick to the (p. 28) healthy before the disease can be propagated. What I propose to consider is the means by which the morbid cause of yellow fever is enabled to part from the body of the patient and to be implanted into that of a healthy person. The need of an external intervention, apart from the disease itself, in order that the latter may be transmitted is made apparent by numerous considerations; some of them already pointed out by Humboldt and Benjamin Rush since the beginning of this century, and now corroborated by recent observations. Yellow fever, at times, will travel across the Ocean to be propagated in distant ports presenting climatic and topographic conditions very different from those of the focus from which the infection has proceeded, while, at other times, the disease seems unable to transmit itself outside of a very limited zone, although the meteorology and topography beyond that zone do not appear to differ very materially. Once the need of an agent of transmission is admitted as the only means of accounting for such anomalies, it is evident that all the conditions which have hitherto been recognized essential for the propagation of the disease must be understood to act through their influence upon the said agent. It seemed unlikely, therefore, that this agent should be found among Micro or Zoophytes, for those lowest orders of animal life are but little affected by such meteorologic variations as are known to influence the development of yellow fever. To satisfy that requisite it was necessary to search for it amongst insects. On the other hand, the fact of yellow fever being characterized both clinically and (according

to recent findings) histologically, by lesions of the blood vessels and by alterations of the physical and chemical conditions of the blood, suggested that the insect which should convey the infectious particles from the patient to the healthy should be looked for among those which drive their sting into blood-vessels in order to suck human blood. Finally, by reasons of other considerations which need not be stated here, I came to think that the mosquito might be the transmitter of yellow fever.

Such was the hypothesis which led me to undertake the experimental investigation which I shall here relate.

The application of the auxiliary sciences to Medicine often demands such a minute acquaintance with the different branches of human knowledge, that one cannot wonder at the length of time which sometimes elapses before certain facts recorded in a special branch can become available for purely medical investigations. This is particularly the case with regard to Natural History; its acquisitions being the outcome of the direct observation of Nature must, as a rule, undergo a complete revision from our own point of view before they can be turned to account in a nosological investigation. It has thus happened that more than a century after Réaumur had written his admirable Memoir on the habits of mosquitoes, justly considered as a model of accurate and keen observation, and which, (p. 29) from a general point of view, appears to exhaust the subject, when, six months ago, I recurred to that valuable source in search of data for the study which I had undertaken, I could not obtain the ones which I most needed. I was consequently obliged not only to go over all the data given by Réaumur, in order to ascertain whether they were also applicable to the Cuban mosquitoes, but to investigate other details about which neither Réaumur nor any other Naturalist had reason to be particularly interested.¹

¹ The truth of these remarks was well exemplified in the case of the mosquito which I had begun to investigate in December 1880, as may be seen from the following notes copied from a slip of paper upon which I had jotted down all the information that I obtained from the accomplished and well-known Cuban Naturalist D. Felipe Poey.

Havana, January 10, 1881, *Culex* mosquito, Robineau Desvoidy, Cuban mosquito. D. Felipe Poey took with him from Cuba to Paris some Cuban mosquitoes in 1817 or 1820, and they were there classified by Robineau Desvoidy.

D. Felipe Poey says that, in the same manner as happens with other insects, the male

Let us first recall the geographical distribution of mosquitoes. They may be said, in general terms, to exist everywhere, except at great altitudes above the sea-level. Many believe that the dipterous insect with which we are concerned, the genus "*Culex*", constitutes a special torment of the tropical regions, while in reality it is found in all latitudes. In the polar regions, the Laplanders, just as the inhabitants of the equinoctial regions of America, are prevented from taking their meals and from lying down to sleep within their huts, unless they surround themselves with an atmosphere of smoke in order to escape those pests. In the open, those insects will fly into their mouths and nostrils, and, notwithstanding the hardening of their skin during the previous winters, they find it necessary to use veils steeped in fetid grease and to anoint their bodies with cream or lard as a protection against mosquitoes. In Canada, in Russia, in England, in France, in Spain, all over Europe, in Siberia, China, the United States, in North and South America, mosquitoes abound. In Central Africa, a German explorer, Dr. Schwinfurst, was tormented by a "spotty-legged" species whose description might agree with that of the Cuban *C. mosquito*; and perhaps also the species observed in Batavia by Arnold, as stated by Dr. Kirby, who considers it as a non-descript variety, not unlike the *C. annulatus*, but without any spots on its wings.

(p. 30) In the same geographical position, however, the mosquito shows a disposition to spread over continents rather than to invade the islands, in accordance with Humboldt's observation that those insects are more abundant along the shores of large

dies after copulation, and the female after laying its eggs. That, in other respects, generation is accomplished under the same conditions as have been described regarding other species.

That the eggs of the Cuban mosquito, deposited upon the water, are black.

That in his opinion, if some mosquitoes do live as long as eight days, it must be because some accident has prevented the union of the male with the female.

The *Culex annulatus* has white rings upon its legs but its body is black; the *C. mosquito*, on the contrary (?), has silvery white plaques upon the last 5 articulations of its 3d pair of legs, 2 ill-defined ones upon the second pair, and two also on the other pair. The abdomen is white underneath. The thorax, he is informed, presents a central longitudinal line.

rivers than upon the islets and that mosquitoes are more troublesome close to the banks than in the centre of rivers. To this circumstance may, perhaps, be due the silence of the first chroniclers of the Discovery of America about mosquitoes, with reference to the first voyages of Columbus.¹ I have not found any mention of them with reference to the Antilles before 1538, when Hernando de Soto's soldiers having to cross a river near Puerto de los Principes, were so severely bitten by mosquitoes that large marks of blood appeared on their backs. To the comparative immunity of islands must probably be attributed the following account given to Osten Sacken (quoted in Brehm, V. IX, p. 446) by an American traveler. In 1823 mosquitoes were unknown on the Hawaiian Isles; but between 1828 and 1830 an old ship from Mexico was abandoned close to the shores of one of those islands. The inhabitants soon noticed around that spot some blood-sucking insects previously unknown to them; and the natives used to come in the evening to allow themselves to be bitten by those extraordinary insects. Mosquitoes afterwards multiplied and spread on those islands, developing into a regular plague.

Although mosquitoes are found in all latitudes, their abundance varies in different localities. Humboldt and Bonpland, in their *Travels in Equinoctial America* wrote: "The annoyance suffered from mosquitoes and "zancudos" in the torrid zone is not so general as most people think. On the high plateaux more than 400 toises (2500 feet) above the sea-level, and in very dry plains, far from large rivers, such as Cumana and Calabozo, gnats are not much more abundant than in the most populous parts of Europe." The influence of dryness and of a long distance from water-courses, pointed out by those travelers, is easily understood, inasmuch as the larvae and pupae of the mosquitoes are aquatic, and the winged insect requires water for the laying and hatching of its eggs. The impediment to their propagation at high levels may consist in the exaggeration of the difficulty which those insects must always experience in flying

¹ This is a mistake, for I have since found the abundance of mosquitoes on the Island Hispaniola specially mentioned in Herrera (*Década I, Lib. V, cap. XI, p. 179*).

upwards after they have filled themselves with blood; a difficulty which will be much more marked in a species having such small wings as those of the *C. mosquito*. The rarefaction of the atmosphere at those great heights necessarily increases that difficulty, and, under those circumstances, the mosquito will instinctively shun those localities. The above mentioned travelers also relate that a missionary priest, Bernardo Zea, had built himself a room over a scaffolding of palm boards, and they (p. 31) used to go there at night to dry their plants and to write their Diary, adding: "The missionary had rightly observed that those insects are more numerous in the lower strata of the atmosphere, within 12 to 15 feet from the ground." Further on they write: "As one proceeds towards the plateau of the Andes, those insects disappear and the air one breathes becomes pure. . . . at a height of 200 toises (1500 feet) mosquitoes and zancudos are no longer feared".

Historically the mosquito is one of the insects most anciently observed. Aristotle and Pliny refer to its proboscis which serves both for piercing the skin and for sucking the blood. The Greek historian Pausanias, according to Taschenberg, mentions the city of Myus, in Asia Minor, situated on a bay which had formerly communicated with the sea but was afterwards cut off from it; when the water in the lake which was thus formed ceased to be salt, such a plague of mosquitoes was developed that the inhabitants had to abandon the city and betook themselves to Miletus. So also in the Decades of Hereera, we read that Juan Grijalva when he first discovered the coast of New Spain (Mexico), in 1518, landed with his men on an islet which he named San Juan de Ulua, and they had to build their huts "at the top of the highest sand-mounds which they could find in order to avoid the importunity of mosquitoes." Seven days later, Bernal Diez del Castillo had to seek protection in some Indian places of worship, "unable to stand the mosquitoes." Finally, in 1519, on the same spot where Veracruz now stands, according to Herrera "the long-legged mosquitoes and the small ones which are still worse used to worry the people who went with Cortes."

I have observed two kinds of mosquitoes in Havana since

December last, when I began to study those insects. One species is large, of a yellowish colour, with thin, long legs, and without any particular markings; I suppose it must be the identical *zancudo* which worried Cortes' men on the sandy plains of San Juan de Ulua in 1519, and the same which La Sagra describes as the *Culex Cubensis*. The length of its body, measured from the root of the proboscis to the anal extremity, varies between 5 and 7 millimetres. This species comes out exclusively at night, generally between 9 and 10 o'clock, and pursues its annoying evolutions until daybreak. All the specimens which I have found inside of mosquito-nets (in the morning) have belonged to that species; and they remain part of the day in that position digesting the blood which they have sucked. The other species is the *Culex mosquito*, specimens of which were taken to Paris by the distinguished Cuban Naturalist, Felipe Poey, in 1817 or 1820, and were there classified by M. Robineau Desvoidy under that name. I have noticed two varieties of this species: one large, with a slight, graceful figure, vigorous, of a dark gray color, somewhat smaller than the *C. Cubensis*; the other only measures from 4 to $4\frac{1}{2}$ millimetres. I have (p. 32) not sought for particular differential characters between these two varieties of the same species, their respective size sufficing for my present object. Both varieties of the *C. mosquito* present the following distinctive characters: the body is dark colored, sometimes almost black or steel-colored; the ventral segments of the abdomen as well as the dorsal ones appear strengthened by an outer layer, with white rings corresponding to the inter-spaces, though sometimes (on the ventral side) the segments are whitish and the inter-spaces are dark. On each side of the abdomen there are two rows of pearly-white dots, between which, after feeding, a transparent membrane stretches allowing the blood or other contents of the distended stomach and intestine to be seen. Upon the hind legs there are five very characteristic white rings, corresponding to the articulations of the tarsus, metatarsus and tibia; the latter sometimes presenting a sixth white spot. The middle and front legs present two or three white rings. Upon the sides of the thorax are seen 8 or 10 white dots or patches of irregular

outline, and upon the antero-superior surface of the thorax a combination of white lines on a dark background is seen resembling a two-stringed lyre. The palps and the antennae also carry some white marks. Some of the aforesaid markings are apt to be effaced with age or by friction, but the most characteristic ones very seldom disappear. The wings of the *C. mosquito*, the venation of which I shall not describe at present, have no spots like those of the European *Culex annulatus*; and its wings are so short that, when closed, they leave the last segment of the body uncovered. Of course, in order to observe the characters which I have been describing it is necessary to use a magnifying glass; aplanatic lenses of $2\frac{1}{2}$ or 3 inches focus are very convenient for that purpose.

The males of both species are readily recognized by their feathery antennae, like a pair of mustachios, and by its three-pronged proboscis due to the long palps which lie close to the proboscis above, but stand out on each side near the point; thereby showing a marked contrast with the smooth proboscis of the female whose short palps barely cover the upper sixth of its length.

The two species of mosquitoes to which I have referred do not come out at the same hours: the zancudo comes out at night and the *C. mosquito* in the daytime. This distribution of the day and night between the two species made me think that the zancudo, notwithstanding its larger size and more robust appearance, might not be constituted to stand the heat of our summer sunshine. I tried, therefore, the following experiment. On the 9th of June, at noon, I exposed to the direct rays of the sun the bulbs of my psychrometer; after half an hour the dry bulb marked 42° . 25 C. and the wet bulb 31° .75. I then substituted in place of the instrument a tube in which a zancudo had been confined for 5 days, but continued (p. 33) lively and agile; after 5 minutes' exposure the insect was dead. I then substituted another tube containing a *Culex mosquito*, and after leaving it exposed to the sun during 15 minutes it was still alive and continued to live another 24 hours in its tube.

It is well known that only the female mosquitoes bite and suck

blood, while the males feed on vegetable juices, principally the sweet ones; but I have not found it mentioned in any author that even the females never bite before having been fertilized. This, at least, I infer from the following experiments.

A female *C. mosquito*, caught soon after breaking loose from its pupa-case, and kept alive during three days, cannot be got to bite during that space of time. I have several times repeated the experiment and always with a negative result.

Female mosquitoes which are caught pairing bite and suck blood readily very soon after they are parted.

Finally, those which are caught in the act of biting and sucking blood, will as a rule, lay eggs after a few days, while the fertilized females which have not been allowed to suck blood die without every laying any ova.

We are thus led to infer that the craving of the female mosquito for live blood is not meant to supply an indispensable article of food. Indeed it seems improbable that for the nourishment of so small a body, such a disproportionate quantity of rich blood be needed. I have come to the conclusion that the sucking of blood is intended for another object connected with the propagation of the species. The likeliest hypothesis seems to be that the feed of blood acts through the degree of heat which it procures. If, for instance, the maturation of the ovules contained in the ovaries of the mosquito demands a temperature of 37°C. , the latter could scarcely be obtained by any other means so readily as by the insect filling itself with a fair amount of blood of that temperature; and sometimes it may be more convenient for the mosquito to bite a patient attacked with fever, whose blood at 39° or 40° may prove more efficacious in hastening the process of ovulation. It will thus be understood why large insects like the zancudo are able to absorb with a single bite the amount of blood required for the maturation of all the 200 to 350 ova which they lay at one sitting, while the smaller species, like the *C. mosquito*, have to bite and fill themselves several times with blood before beginning to lay, and generally require several sittings before all their ova are laid.

After the female mosquito has filled itself with blood it requires

two, three or four days, according to the species (*and the season of the year*) to complete the digestion of its feed; and, during that time, remains out of sight spending hours in a curious performance the object (p. 34) of which Réaumur did not understand, having only observed it in the open. When the insect is confined in a glass tube, it is easy to see that the performance consists in besmearing every part of its body with a secretion which is picked up from the anal extremity with its hind legs and smeared successively upon the legs, the abdomen, the wings, the thorax, the head and even the proboscis. As suggested by Felipe Poey, *facile princeps* among our Cuban Naturalists, the object of this operation is probably to make the mosquito water-proof before it goes to the water to lay its eggs. During the digestion, the mosquito also drops some bloody particles or excrement which present the peculiarity of being extremely soluble in water, even after being kept in a dry condition during several months. This is probably due to the admixture of the blood with the saliva poured out during the process of biting, and which is generally believed to render the blood more fluid while it is being sucked by the insect. As a rule after a complete, uninterrupted feed of blood, the mosquito does not bite again, and even shuns the contact of the bare skin (perhaps because the heat of it becomes at that time disagreeable) until the digestion of the blood has been completed. With the zancudo (night-mosquito) it is at that time that its ova are laid.

I shall not reproduce the classical description given by Réaumur of the manner in which the female of a European species, *Culex pipiens*, builds its tiny boat of eggs and floats it on the water. The *zancudo* of Cuba goes through a similar performance; but after having launched their little boat of eggs, they often stretch themselves out to die upon the water, and I have wondered whether the dead insects which Réaumur attributes to newborn ones which have been wrecked and drowned at the moment of leaving their pupa-shell might not be the cadavers of mothers who had died in order that their bodies should remain close to the ova so as to contribute to the feeding of their progeny.

The three successive operations: fertilization, sucking of blood

and laying of eggs, constitute the most essential phases of the mosquito's existence. The first of these operations, as in most other insects, probably, need not occur more than once in order that the impregnated seminal sack of the female shall retain the faculty of fertilizing all the ova which may thereafter traverse its oviducts. In the Cuban bee, according to Felipe Poey, a single fecundation by the male, suffices for all the thousands of eggs which the female bee lays during the two or three years of its life. With the females of the various species of the genus *Culex*, which, till now, had been observed, there had been no occasion to test whether such a prolonged fertilizing faculty existed, inasmuch as all their ova were laid at a single sitting; but the case is different with the females of the *Culex* mosquito. These lay their ova separately or in files of 9 to 15 either isolated or in groups, sometimes upon the water (p. 35) or else upon solid bodies not too far removed from the level of the water, so that a moderate elevation of that level will allow the water to cover them. My explanation about the need of several bites and feeds of blood before the *C. mosquito* is able to lay all its ova, maybe purely hypothetical; it is nevertheless a fact that the females of that species are always ready to bite a second time after they have digested all the blood which had been sucked at a previous bite. A female *C. mosquito*, caught (in Havana) in January of the present year, had bitten 12 times and laid eggs three times in the course of the 31 days which it lived; its death having occurred in New York where it was exposed to temperature below the freezing point.

With the captive females of the *C. Cubensis* (*C. Pungens*), I have never been able to obtain a second bite, whether it had or had not laid its ova. Possibly, however, when at large they may need to bite several times before laying; for I have occasionally seen them come to bite my hand, with some blood already in their stomach. This I have attributed to a previous bite which had been interrupted before the insect had been able to draw its full allowance of blood.

Evidently, from the point of view which I am considering, the *Culex* mosquito is admirably adapted to convey from one person

to another a disease which happens to be transmissible through the blood; since it has repeated opportunities of sucking blood from different sources, and also of infecting different persons; so that the probabilities that its bite may unite all the conditions required for the transmission will thereby be greatly increased. On the other hand, inasmuch as the *C. Cubensis* absorbs a larger quantity of the infectious blood at each feed, its mouth-parts may retain a larger amount of virus, and perhaps produce a graver inoculation when it happens to attack a non-immune a few moments after having bitten the patient, its first bite having been interrupted. In that case, a graver infection might result but the chances of its occurring would be much less.

In order to understand the special facilities which the bite of the *C. mosquito* affords for the inoculation of any infectious particles which should be contained in the blood, it is necessary to have some idea of the disposition and structure of the apparatus used by the female mosquito in its operation of stinging and of sucking blood.

What is seen of the proboscis, under ordinary circumstances is the sheath, which represents a modified nether lip. It arises from a pedicle attached to the base of the head, below the other mouthparts. It is slit along its upper border as far as the terminal, conical button seen at its free end, and which, I believe, is formed by two labial palps. From the extremity of this button the other pieces constituting the sting are protruded (in the act of stinging). The sheath of the *C. mosquito*, to (p. 36) which species my observations have been limited, measures $2\frac{1}{2}$ millimeters; that of the species observed by Réaumur measured according to that author, *one French line*; and as our mosquito oftentimes drives its sting nearly to its very root, it can readily reach a blood-vessel at a depth not exceeding $\frac{1}{5}$ of a centimetre. In the interior of the sheath are two tubes, lying apparently loose at the bottom of its concavity; I have observed them presenting a tortuous direction, and uniting into a common trunk within the concavity of the pedicle. I believe it is through these tubes that the mosquito pours out the acrid saliva which causes the burning sensation during its bite, and which, according to

naturalists, serves to render more fluid the blood which has to run through the sucking apparatus.

Within the sheath are contained five pieces: the principal one constitutes the labrum or upper-lip, it is of a horny consistence and prolonged like a long spur, deeply grooved so as to form a canal opening upwards¹ and ending in a point like that of a tooth-pick cut out of a long slender quill. This piece is rigid and presents on its outer surface a curious design as if covered with a net whose meshes, in relief, form small parallelograms with acute angles pointing longitudinally. Perhaps within those innumerable meshes might be lodged some particles of the blood sucked by the insect. The other four pieces are paired, flexible setae, two of them constituting the mandibles, and the others the maxillae. The structure of the two pairs is very different in each. The mandibles are concave inwardly, and have a tendency to maintain a curvilinear direction; their outer side is convex and presents transverse ridges ending on their free border in very minute teeth. The point of the mandibles is curved and armed to its very end with teeth which appear to be both sharp and strong. The maxillae are inserted a little below the mandibles; they present the appearance of a ribbon with its edges turned in like a seam, armed with a fringe of long delicate teeth; its general aspect is that of a long narrow blade of grass, ending in a broad double-edged point and strengthened by a longitudinal vein running all along its middle. All these setae adapt themselves upon the stem of the labrum so closely that, after the sheath has been removed and before the setae are dissociated, one would never think that the round or oval rod, with its sharp, single point, which comes into view is an assemblage of the five separate pieces which I have been describing.²

¹ This is a misprint. It should read "downwards."

² The above description was written under the impression that only 5 mouth parts went to constitute the sting of the *Culex* mosquito, and of mosquitoes in general. Soon after writing this paper, however, I became aware of the existence of a sixth seta, in accordance with the statements of modern entomologists.—On closer observation too, I found that what I had described as one of the mandibles, more properly applies to the hypopharynx, about the existence of which I was at that time ignorant. I append therefore a reproduction of a drawing which I made in 1882 or 83 of the six mouth parts of the

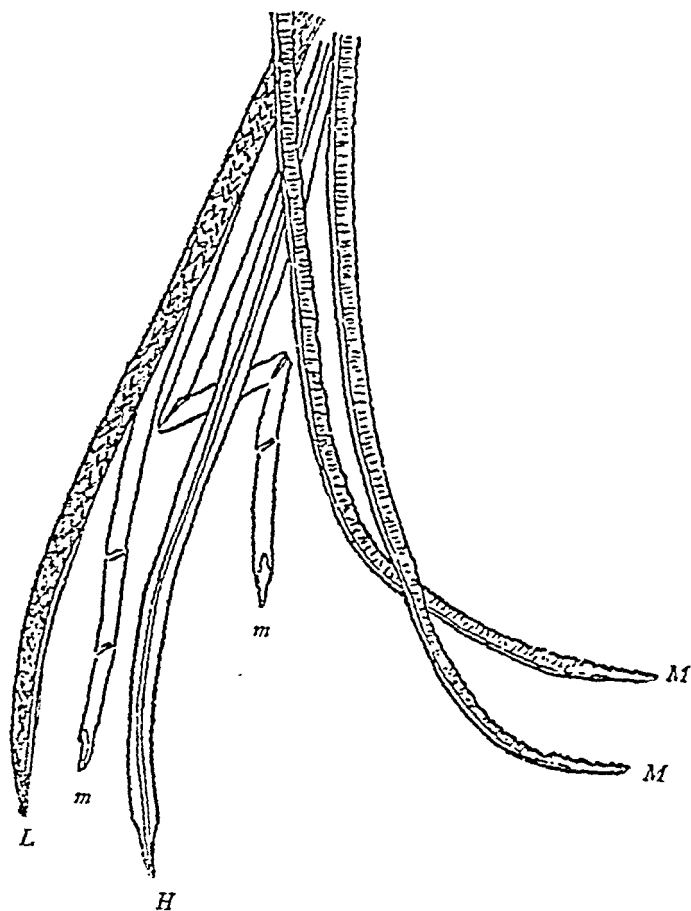
The mosquito commences its operation of stinging by tentatively exploring the skin with the point of its proboscis until it finds a suitable spot. It then takes a firm position upon its six feet (sometimes the two hind legs are raised above its back), the thorax is strongly bent down while the head and the proboscis assume a vertical position. Next, with the naked eye or, better, with the assistance of a magnifying glass, the sheath is seen to bend backwards, at its upper part, gradually assuming the shape of an horizontal < the two branches of which gradually come closer together as the sting penetrates deeper into the skin. The sting is then seen as a very slender wire stretching between the extremities of the horizontal < figured by the sheath, and moving up and down in unison with the maxillary palps, until a blood-capillary has been reached. The insect remains motionless while it fills itself, apparently without effort, with the red warm blood of its victim. During the bite a sharp, instantaneous, burning sensation is sometimes felt, owing to the saliva which the mosquito instils into the wound through the end of the sheath, the conical extremity of which remains caught between the edges of the wound. The insect's stomach becomes distended and the blood is seen through the transparent lateral walls of its body. Several minutes are generally required for the completion of the operation; as long as seven in some cases which I have timed.

It is a well-known fact that, while mosquitoes are never wholly absent (p. 38) from Havana, they are much more abundant at some seasons of the year. It appears to me that they increase in numbers from April or May till August, and thereafter gradually decrease till February or March. Another point, however,

sting.—Regarding the existence of one or two tortuous tubes with striated walls, occupying the concavity of the sheath, and which I considered as the excretory duct of the salivary glands, I have met with it on several occasions and still believe that in the species which I am considering the salivary duct may not empty itself into the tube of the hypopharynx, but runs through its base lying free in the concavity of the sheath. This supposition has been strengthened in my mind by a precedent which I have just read in Packard's Text-Book of Entomology, p. 78 where he quotes from Meinert the following:

"The efferent duct of the thoracic salivary glands (ductus salivalis) perforates the hypopharynx, more or less near the base, that the saliva may be ejected through the canal into the wound, or that it may be conducted along the labellæ. *Very rarely the salivary duct perforating the hypopharynx, is continued in the shape of a free, very slender tube.*"

requires to be borne in mind, inasmuch as it affords an explanation of the recurrence, hitherto unaccounted for, of yellow-fever epidemics without new importation, in localities previously considered as immune. I allude to the hibernation of mosquitoes, a phenomenon which is not observed in our climate, at least in



L, labrum; *m*, maxillae; *H*, hypopharynx; *M*, mandibles

all its phases; but which constitutes, according to the best authorities, the regular mode by which the species is propagated in cold climates, during winter. Taschenberg informs us that: "the fertilized females of the last generation hibernate during winter in out-of-the-way places such as the cellars of dwellings, and set about propagating their species the following spring."

Among the conditions which favor the development of mosquitoes may be mentioned; heat, moisture, the vicinity of stagnant waters, low, dark localities sheltered from the wind, and the summer-season. It is necessary, however, to bear in mind Humboldt's observation that the abundance of mosquitoes is not always in accordance with recognizable meteorological or topographical conditions.

I have already referred to the difficulty which our mosquito, by reason of its comparatively small wings, must experience in its upward flight after it has filled itself with blood. It will also be hindered by the same cause, from going far from the place where it has accomplished its last bite, and, in general, from traveling any considerable distance through the air without resting. This circumstance will not prevent, however, its being conveyed, hidden among clothes, caught under a hat, inside of a traveling bag, etc., to considerable distances, after a recent bite, perhaps carrying upon its mouth-parts the inoculable germ of the disease.

The preferences which mosquitoes show for certain races and individuals should also be borne in mind; the African race being, apparently, the one least tormented by them, and the greatest sufferers being the Northern races newly arrived in the tropical regions of America. It is probable that this may be due to the comparative thickness of the skin, and to peculiarities in the cutaneous capillary circulation, since those circumstances must influence the facility with which the female mosquito will be able to procure itself the blood which it requires in order to accomplish its life-cycle.

After this long, but necessary account of the habits of our Cuban mosquitoes, and of the *Culex* mosquito in particular, let us consider by what means that insect might transmit the yellow fever, if that disease happens to be really transmissible through the inoculation of blood. The first and most natural idea would be that the transmission might be effected (p. 39) through the virulent blood which the mosquito has sucked, amounting to 5 and even to 7 or 9 cubic millimeters, and which, if the insect happens to die before completing its digestion, would be in ex-

cellent condition to retain during a long time its infecting properties. It might also be supposed that the same blood which the mosquito discharges, as excrement, after having bitten a yellow fever patient, might be dissolved in the drinking water, whereby the infection might be conveyed if the latter were susceptible of penetrating by the mouth. But the experiments of Ffirth and other considerations arising from my personal ideas regarding the pathogenesis of yellow fever, forbid my taking into account either of those modes of propagation, as I shall now explain. When the U. S. Yellow-fever Commission took their leave, two years ago, they presented us with a valuable collection of micro-photographs from preparations made by our corresponding Member, Dr. Sternberg, showing what, to me, appeared to be a most striking feature, namely, that the red blood-globules are discharged unbroken in the hemorrhages of yellow-fever. This fact taken in connection with the circumstance that those hemorrhages are often unattended with any perceptible break in the blood-vessels, while, on the other hand, they constitute a most essential clinical symptom of the disease, led me to infer that the principal lesion of yellow fever should be sought for in the vascular endothelium. The disease is transmissible, it attacks but once the same person, and always presents in its phenomena a regular order comparable with that observed in the eruptive fevers, all of which circumstances suggested to my mind the hypothesis that yellow-fever should be considered as a sort of eruptive fever in which the seat of the eruption is the vascular endothelium. The first period would correspond to the initial fever, the remission to the eruptive period, and the third period would be that of desquamation. If the latter phase is accomplished under favorable conditions, the patient will only show evidence of an exaggerated transudation of some of the liquid elements of the blood through the new endothelium; if the conditions are unfavorable, a defective endothelium will have been produced, incapable of checking the figured elements of the blood: passive hemorrhages will occur and the patient may find himself in imminent danger. Finally, assimilating the disease to small-pox and to vaccination, it oc-

curred to me that in order to inoculate yellow fever it would be necessary to pick out the inoculable material from within the blood vessels of a yellow-fever patient and to carry it likewise into the interior of a blood vessel of the person who was to be inoculated. All of which conditions the mosquito satisfies most admirably through its bite, in a manner which it would be almost impossible for us to imitate, with the comparatively coarse instruments which the most skillful makers could produce.

Three conditions will, therefore, be necessary in order that yellow (p. 40) fever may be propagated: 1. The existence of a yellow fever patient into whose capillaries the mosquito is able to drive its sting and to impregnate it with the virulent particles, at an appropriate stage of the disease. 2. That the life of the mosquito be spared after its bite upon the patient until it has a chance of biting the person in whom the disease is to be reproduced. 3. The coincidence that some of the persons whom the same mosquito happens to bite thereafter shall be susceptible of contracting the disease.

The first of these conditions, since Dr. Ambrosio G. del Valle has been publishing his valuable mortuary tables, we may be sure, has never failed to be satisfied in Havana. With regard to the 2d and 3d, it is evident that the probabilities of their being satisfied will depend on the abundance of mosquitoes and on the number of susceptible persons present in the locality. I firmly believe that the three above mentioned conditions have, indeed, always coincided in years when yellow fever has made its greatest ravages.

Such is, Gentlemen, my theory; and I consider that it has been singularly strengthened by the numerous historical, geographical, ethnological and meteorological coincidences which occur between the data which I have collected regarding the mosquito and those which are recorded about the yellow fever; while, at the same time, we are enabled by it to account for circumstances which have until now been considered inexplicable under the prevailing theories. Yellow fever was unknown to the white race before the discovery of America, and, according to Humboldt, it is a tradi-

tional opinion in Vera Cruz that the disease has been prevailing there ever since the first Spanish explorers landed on its shores. There also, as we have seen, the Spaniards since their first landing have recorded the presence of mosquitoes; and with greater insistence than in any other place in America, in the identical sand-mounds of San Juan de Ulloa (the present site of Veracruz). The races which are most susceptible to Yellow fever are also the ones who suffer most from the bites of mosquitoes. The meteorological conditions which are most favorable to the development of yellow fever are those which contribute to increase the number of mosquitoes; in proof of which I can cite several local epidemics regarding which competent authorities assert that the number of mosquitoes during the prevalence of yellow fever was much greater than on other occasions; indeed, it is stated in one instance that the mosquitoes were of a different kind from those which were usually observed in the locality, having gray rings around their bodies. Regarding the topography of the yellow fever, Humboldt points out the altitudes beyond which mosquitoes cease to appear, and in another passage gives the limits above the sea-level within which the yellow fever may be propagated. Finally, in the notorious case of the U. S. Steamship Plymouth, in which two cases of yellow fever occurred at sea, after the vessel had been disinfected and frozen during (p. 41) winter, four months after the last previous case had occurred on that vessel (the preceding November), the facts can be readily accounted for by the hibernation of mosquitoes which had bitten the former yellow fever patients, and, which, upon finding themselves again within tropical temperatures, recovered from their lethargic condition and bit two of the new men of the crew.

Supported by the above reasons, I decided to submit my theory to an experimental test, and, after obtaining the necessary authorization, I proceeded in the following manner.

On the 30th of last June, I took to the Quinta de Garcini a mosquito which had been caught before being allowed to sting, and there made it bite and fill itself with blood from the arm of a

patient, Camilo Anca, who was in the fifth day of a well characterized attack of yellow fever of which he died two days later. I then picked out F. B., one of twenty healthy non-immunes who have continued until now under my observation, and made the same mosquito bite him. Bearing in mind that the incubation of yellow fever, in cases which allow its limits to be reckoned, varies between one and fifteen days, I ordered the man to be kept under observation. On the 9th of July, F. B. began to feel out of sorts, and on the 14th he was admitted to the Military Hospital with a mild attack of yellow fever perfectly characterized by the usual yellowness, and albumin in the urine which persisted from the third till the ninth day.

On the 16th of July, I applied a mosquito at the same Quinta de Garcini, to a patient, Domingo Rodríguez, in the third or fourth day of yellow fever; on the 20th, I allowed the same mosquito to bite me and, finally, on the 22nd I made it bite A. L. C., another of the 20 men who are under observation. Five days later, this man was admitted at the Hospital with fever, severe headache, pain in the loins and injected eyes; these symptoms lasted three days, after which the patient became convalescent without having presented any yellowness nor albuminuria. His case was, however, diagnosed as "abortive yellow fever" by the physician in charge.

The 29th of July, I made a mosquito bite D. L. R. who was going through a severe attack of yellow fever at Quinta de Garcini, being then in its third day. On the 31st, I made the same mosquito bite D. L. F., another of my 20 men under observation. On the 5th of August, at 2 a. m., he was attacked with symptoms of mild yellow fever; he subsequently showed some yellowness but I do not think that he developed any albuminuria; his case was, nevertheless, diagnosed "abortive yellow fever."

Finally, on the 31st of July, I applied another mosquito to the same patient, D. L. R. at Quinta Garcini, his attack having then reached its fifth day and proving fatal on the following one. On the 2d of August I applied this mosquito to D. G. B., another of my twenty non-immunes. Till the (p. 42) present date (12th)

this last inoculation has not given any result; but, as only 12 days have elapsed, the case is still within the limits of incubation.¹

I have to state that the persons mentioned above are the only ones who were inoculated with mosquitoes, in the manner described; and that since June 12th, till now (in the course of seven weeks), barring my first three inoculated men, no other case of confirmed or abortive yellow fever has occurred among the twenty non-immunes, whom I have had under observation.²

These experiments are certainly favorable to my theory, but I do not wish to exaggerate their value in considering them final, although the accumulation of probabilities in my favor is now very remarkable. I understand but too well that nothing less

¹ This inoculated man D. G. B., came to my office on the 17th of August to be inspected, stating that during the previous six days he had been suffering from headache, loss of appetite and general malaise. On the 24th I found that he had fever (Pulse 100, Temp. 30.1), and he stated that it had been higher on the previous day and also that same morning. The fever however was never severe, and the patient did not report himself sick nor take any medicine. The fever ceased, but the pain in the head continued a few days longer.

Another of my 20 non-immunes was bitten on the 15th of August by a mosquito which, 2 days before, had bitten a patient in the Military Hospital, in the 5th day of yellow fever. This inoculated man does not appear to have been sick so far (September 1st). I have not been able to see him since his inoculation, and it is only from hearsay that I have been informed that he has felt poorly on the 24th and 25th of August; but did not report himself sick.

² There was a fourth case which was also diagnosed as "abortive yellow fever" at the Military Hospital, but regarding whose diagnosis Dr. Delgado and I were doubtful. He was one of the 20 non-immunes of our group, and a different kind of inoculation was tried upon him, the particulars of which will be considered of some interest at the present day.—On the 28th of June 1881, 7 a.m., a night mosquito (*C. pungens*) was found inside the mosquito-net of a fatal case of yellow-fever, in the 5th day of attack. Placed in a glass cage, the *pungens* discharged some black blood upon the sides of the tube, the following day. On the 26th of July, a couple of drops of sterilized distilled water was used to dissolve the dry bloody excrement and the same was soaked up with a small bit of sugar, which looked thereafter as if it had been soaked in black coffee. A freshly caught *C. mosquito* was now introduced in the phial, and went greedily for the sugar. A little more water was now added, turning the sugar into a reddish brown syrup, from which the same *C. mosquito*, in the course of $\frac{1}{2}$ hour had taken a good feed.—On the 29th of July, 2 p.m., L. G. P. one of my 20 non-immunes, was bitten by this *C. mosquito*.—On the 31st of July this man was admitted to the Military Hospital with fever, flushed face, cephalalgia, pain in the back, epigastralgia, injected eyes.—On the 3d of August he had neither fever nor albumin.

than an absolutely incontrovertible demonstration will be required before the generality of my colleagues accept a theory so entirely at variance with the ideas which have until now prevailed about yellow-fever. In the mean time, I beg leave to resume in the following conclusions the most essential points which I have endeavored to demonstrate.

(p. 43)

CONCLUSIONS

1. It has been proved that the *C. mosquito*, as a rule, bites several times in the course of its existence, not only when its bite has been accidentally interrupted, but even when it has been allowed to completely satisfy its appetite; in which case two or more days intervene between its successive bites.

2. Inasmuch as the mouth-parts of the mosquito are very well adapted to retain particles that may be in suspension in the liquids absorbed by that insect, it cannot be denied that there is a possibility that said mosquito should retain upon the setae of its sting some of the virulent particles contained in a diseased blood, and may inoculate them to the persons whom it afterwards chances to bite.

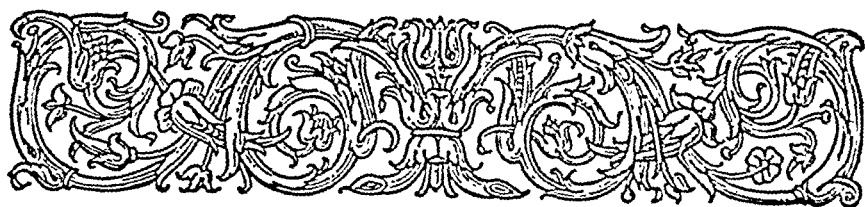
3. The direct experiments undertaken to decide whether the mosquito is able to transmit yellow fever in the above stated manner, have been limited to five attempted inoculations, with a single bite, and they have given the following results: One case of mild yellow-fever, perfectly characterized, with albuminuria and icterus; two cases diagnosed as "abortive yellow fever" by the physicians in charge; and two ephemeral fevers without any definite characters. From which results it must be inferred that the inoculation with a single bite is insufficient to produce the severe forms of yellow fever, and that a final decision as to the efficacy of such inoculations must be deferred until opportunity is found for experimenting under absolutely decisive conditions, outside of the epidemic zone.

4. Should it be finally proven that the mosquito-inoculation not only reproduces the yellow fever, but that it constitutes the regular process through which the disease is propagated, the conditions of existence and of development for that dipterous insect

would account for the anomalies hitherto observed in the propagation of yellow fever, and while we might, on the one hand, have the means of preventing the disease from spreading, non-immunes might at the same time be protected through a mild inoculation.

My only desire is that my observations be recorded, and that the correctness of my ideas be tested through direct experiments. I do not mean by this that I would shun the discussion of my opinions; far from it, I shall be very glad to hear any remarks or objections which my distinguished colleagues may be inclined to express.¹

¹ N. B. The notes do not belong to the original paper.—C. F.



Yellow Fever: Its Transmission by Means of the Culex Mosquito

BY

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IN THE month of May, of last year, when the yellow fever epidemic was commencing at Vera Cruz, Dr. Carmona, of Mexico, inoculated six prisoners with the dried residue of yellow fever urine. In two of the six, the local symptoms of the inoculation were immediately followed by those of fatal yellow fever, and, a few days later, both died *on the same day* (Carmona, *Leçons sur l'étiologie et la prophylaxie de la fièvre jaune*, p. 265). This unfortunate result agrees with the views I have entertained since 1881, viz., that whereas the disease is not spontaneously transmissible by infection through the air nor by contact, it can be communicated by inoculation. In searching for a natural agent capable of fulfilling this condition, I was led to fix upon the Culex mosquito as the most likely one. Before submitting, however, the experimental results which, so far, appear to confirm my theory, it will be necessary to describe the habits and peculiarities of this insect.

Most books on natural history inform us that only the *female* mosquito stings human beings and animals for the purpose of sucking their blood, the *males* feeding only on sweet juices or nutrient liquids. The fecundated females, in cold climates, hibernate during winter, in a state of apparent death, in dark

corners, in cellars, etc., to revive with the return of warm weather, when they will lay eggs and propagate their species. I was unable, however, to ascertain from previous writers whether gnats, in general, suck blood more than once, how long they live after their first bite, and many other particulars essential for my investigation. I was, therefore, obliged to undertake a systematic study of the species generally found in Havana, to which alone the following remarks must be understood to apply, leaving future inquiries to determine (p. 396) whether the same may be true of others that are known to exist in the interior of the island and in foreign countries.

Two species of mosquitoes are commonly observed in Havana. One, the *Culex cubensis* (La Sagra), *zancudo*, or long-legged mosquito, is from five to six mm. in length, of a yellowish or fawn color, with long, thin legs, and no noticeable spots upon its body or legs. This species is nocturnal, coming out exclusively at night and retiring before daybreak; they are often found in the morning, in a state of torpor, gorged with blood, inside of mosquito nets. I have never succeeded in getting these *zancudos* to sting a second time after they had once become filled; but as they can be kept alive, by feeding with sugar, over a period of forty days, it is unlikely that they should not bite more than once when in a state of freedom. The female of this species lays its eggs pretty much in the same manner as the European gnat, described by Reaumur, forming a boat-like aggregate of eggs, where over one hundred are closely packed together, standing upright, side by side, the tiny raft being left floating upon the water.

The other species is the *Culex* mosquito (Robineau Desvoidy), lately described, I am told, as "*Culex fasciatus*." There are several varieties, principally distinguishable by their dimensions and shades of color; some being small and nearly black, while others are stronger, almost as large as the nocturnal species, and of a brown or steel color; the general characteristics being the same in the two or three varieties that I have observed.

The body of the *C. mosquito* is dark colored, the ventral surface coated with a thick skin and marked with gray or white rings; on each side of the abdomen is a double row of white dots,

between which stretches a transparent membrane through which the blood can be seen when the insect is full. The most striking feature consists in five white rings on its hind legs, corresponding to the tarsal and metatarsal articulations. Others less apparent are on the fore and middle legs; white spots are visible on the sides of the thorax and front of the head, while the corselet presents a combination of white lines in the figure of a two-stringed lyre. The wings, when closed, do not cover the end of the body.

The *males* are known by their bushy antennae and long palps lying close to the proboscis, and curved outward near the point; whereas the *females* have delicate antennae and short palps drawn up close to the root of the proboscis.

The female of this species lays its eggs in a different manner from the *zancudo*, not in a boat-like aggregate but singly, having previously deposited a viscous substance through which they lie scattered in irregular groups, either upon the liquid surface or upon the sides of the vessel, close to the water's edge.

The above details are easily made out with the aid of a magnifying (p. 397) glass. I need not enter upon a minute description of the six pieces which constitute the sting of the female mosquito (labrum, mandibles, maxillae, and tongue); suffice it to say that, in the act of biting¹ and sucking blood it represents a hollow lance, from 2 to 2½ mm. long, 1/30 mm. broad at its base and about 1/40 near its extremity. The point is shaped like that of a writing pen, its edges being provided with ten or twelve sharp teeth decreasing in size as they reach the finely pointed extremity. The shaft presents transverse serrated ridges, which must act somewhat like the teeth of a conical file; these ridges, as well as the terminal teeth, belonging to the mandibles which are closely applied upon the sides of the labrum.

The sting remains enclosed in a brown, hairy sheath, excepting when it is introduced into the skin; during this operation, the sheath, which is slit in front to within a short distance of its point, bends backward and the sting appears like a fine wiry lance. This generally penetrates to a depth of from 1½ to 2 mm. before a

¹ This term is used in accordance with general custom notwithstanding its obvious inaccuracy.

bloodvessel is reached of sufficient calibre to allow blood to be drawn. The insect requires from one to five or seven minutes to complete this operation. When once it has fairly implanted its sting, the mosquito can be easily covered with a glass tube or phial and imprisoned. I have generally resorted to this means in order to procure live specimens, so as to be sure of their efficacy for my experiments.

The *C. mosquito* is diurnal and crepuscular, making its appearance early in the morning, again between 9 and 10 a. m., and in the afternoon until night. Stragglers may be met as late as 10 or 11 p.m., and in close, dark rooms they are generally felt or heard throughout the day (in summer). The males are the first to make their appearance, apparently attracted by the emanations of human perspiration from the body or from worn clothes; they keep flying about until the females appear, and it is only after pairing that the new females are able to sting and draw blood. When caught as they emerge from their pupa-case, they often attempt to do so, but their proboscis bends, either from want of rigidity of the sheath, or from obstruction at its point, and the lance fails to pierce the skin. Immediately after pairing, however, the insect is ready to sting.

I have found no difficulty in getting this species to do so as often as it has completed the digestion of the blood previously sucked, but not before an interval of from two to five days (according to the season and the weather), when the insect had been able to fill itself completely. As a proof of the remarkable resistance of this insect to rough usage, and in order to exemplify some of its habits, I copy the following record from my notebook:

(p. 398) *January 13, 1881.* A fresh female *C. mosquito* was caught in the afternoon and allowed to fill with blood off my hand, being retained captive in a glass tube closed with a muslin cap.

15th. Filled again from my hand, biting through the muslin cover.

16th. Strong and active; still distended with blood, refuses to sting.

17th. Stings my hand readily through the muslin and fills.

18th. Though still retaining some blood, bites my hand readily through the muslin. Two hours later, not having apparently taken its usual quantity of blood at the previous bite, it stings again and sucks during two minutes. (Probably the interposition of the muslin interferes with the act of sucking.) At this period, knowing that only the fecundated females draw blood, I introduced a small quantity of water into the phial, in order that eggs might be laid. The insect immediately goes to the water, and after discharging a whitish viscid substance upon the sides of the tube, deposits some white eggs, close to the edge of the water. Six of them were disposed vertically one above the other. The rest of the day the insect was busy besmearing every part of its body (legs, wings, and head included) with a viscid substance collected with the hind legs from the posterior extremity of the body. The white eggs turned black after some hours.

19th. Continues laying eggs.

20th. More eggs; some upon the sides of the phial; stings my hand and sucks readily. The water becomes colored red from the excrementitious particles discharged into it.

21st. Refuses to sting; has lost its left hind leg.

22d. Still laying. One small wriggler has been hatched. Cannot be got to sting.

23d. More eggs laid. Refuses to sting.

24th. The water is teeming with wrigglers. The insect was now transferred to another phial with water. Stings my bare hand very readily, taking about seven and a half minutes to fill.

25th. Refuses to sting. No new eggs.

26th. Bites readily, but, unable to reach a bloodvessel, withdraws its sting, and after feeling the surface of the skin, finds a more convenient spot, where it fills completely.

27th. Refuses to sting. In moving the phial the insect was soaked by the water, but recovered.

28th. Has laid over fifty eggs since yesterday evening; bites readily, and fills from my hand.

29th. Refuses to sting. No new eggs. Most of the white marks upon the body of the mosquito have nearly disappeared.

31st. Bites readily, and fills from the palm of my hand.

February 2. Bites, and fills from my thumb. Having been transferred to another phial with fresh water, was found lying partly submerged and motionless. On filtering off the water the insect revived. It was then transferred to a new dry phial for the purpose of continuing the observations during my trip to New York.

3d. Still retains some black blood; has lost its left foreleg.

4th. Bites, and fills from my hand. Taken on board of the steamer starting for New York.

5th. Refuses to sting.

6th. Bites, and fills readily.

(p. 399) *7th, 8th, 9th, 10th.* Alive, but refuses to sting. The weather was quite cold, the last three days passed off Sandy Hook.

12th. The phial, packed in a valise, was sent by express to Orange, N. J.; the insect arrived nearly dead.

13th. Dead, after thirty-one days captivity, having bitten twelve times, and laid probably over two hundred eggs.

From inquiries made on the steamer, I ascertained that mosquitoes are rarely felt on board during the three or four days that the vessel is detained in the port of Havana, where she lies at a distance from the wharves. In New York, where the ship goes to the wharf, they are apt to be more troublesome, but generally disappear soon after the vessel has left the port.

Mosquitoes are observed in Havana all the year through, but much more so from May to October. In winter they are rare when the temperature falls below 70° F. Last year (1885) has been an exception to the general rule. Mosquitoes, especially the diurnal species, were difficult to procure throughout the summer; but became more numerous in the latter part of September, October, and November. A remarkable scarcity of yellow fever cases was likewise observed in the summer months, and I called attention to this coincidence at one of the sessions of our Academy. In October and November more cases of the disease were signalled, both in hospital and private practice, than in the previous months of the year, although the summer heat had been

more intense than usual, and had abated toward the end of September, in October and November the weather being quite mild.

Although great differences are observed in the duration of the successive phases of development of the *C. mosquito*, the following data may be taken as a fair average: Every mosquito that stings may be considered as a fecundated female, and will probably lay eggs within a few days after its bite, provided it can find water upon which to lay them. In water-jugs standing in bedrooms, the insect is often found depositing its eggs either on the sides of the jug or upon the water. The eggs are commonly hatched, producing minute wrigglers, between the second and fourth day, in summer; some are delayed much longer, and those that are deposited outside the water may remain a long time in the dry state without losing their vitality. The wrigglers grow more or less rapidly according to the nutritive material contained in the water, the temperature, etc., but they probably pass into the pupa stage within twelve or fourteen days. This stage is always short, not lasting more than two or three days, the fully developed mosquito emerging from its aquatic case a fortnight or three weeks after the egg was laid.

From the above data it will be understood how a single infected mosquito, which happens to be conveyed to a healthy locality, when the temperature and altitude are appropriate, might, if my theory be true, (p. 400) inoculate the disease to any liable subject whom it should there sting; and, according to the usual rate of incubation, at the end of a fortnight or three weeks, the consequent attack of yellow fever would be at its height. In the meantime the imported insect would have produced a whole brood of its own species, probably in the vicinity of the place where the patient is lying; thus providing the necessary conditions for the subsequent propagation of the disease.

It remains, therefore, to be determined whether the limits of temperature and of altitude within which the *C. mosquito* is able to exert its functions, agree with those which are known to limit the propagation of yellow fever. The following simple experiments appear conclusive on these points:

1. Let a female *C. mosquito*, of medium size, be placed in a test-tube with a thermometer passing through the cotton-plug, and the tube dipped in water, the temperature of which is gradually lowered by the addition of ice and salt. The following effects will be observed:

Between 66° and 60° F., the insect is benumbed, scarcely moving, sometimes falling to one side in a state of apparent death.

Between 60° and 32° F., apparent death more pronounced.

If the water be allowed to return to its former temperature:

Between 60° and 65° F., the insect shows signs of life.

Between 65° and 68° F., it is able to walk and fly.

Above 77° F., it recovers its former agility, but is at first unable to bite; indeed, if the cooling has reached 32° F., or below, the insect generally dies within a short time.

The larger varieties seem, however, to bear low temperatures better than the small, and a difference is observed according as the change is effected more or less rapidly.

2. In order to test the limits of heat, let a test-tube, similarly disposed, with a thermometer and live mosquito, be suspended inside of a large empty flask, standing in a basin of hot water. The following effects will be noted:

Between 95° and 100° F., the insect appears uncomfortable.

Between 102° and 105° F., remains motionless in apparent death, but is apt to recover and to sting again when restored to a normal temperature.

From 105° to 110° F., apparent or actual death; the insect, if it does revive, not being able to sting again, and generally dying within a few hours.

3. As regards barometric pressures, the experiment would best be tried in such localities as Vera Cruz, Orizava, and Mexico, or in Rio Janeiro and the heights near it, but, failing that resource, I have contrived the following plan:

A female *C. mosquito* is placed in an empty bottle connected with an aneroid barometer, and a suction flask raised to a proper height:

At rarefied pressures corresponding to 2000 or 3000 feet, the

insect becomes at first unable to fly, but if withdrawn will bite and draw blood after a while.

At rarefied pressures corresponding to 4000 or 6000 feet, the the general effects are more marked, but the insect does not die, and seems even to (p. 401) get accustomed to the new state of things; but when withdrawn continues weak, and unable to sting for several hours.

We are thereby led to infer that the *C. mosquito*, when suddenly transferred to heights above 3000 or 4000 feet, must find it difficult to exert its functions, and that it would never, of its own accord, seek elevations which render its flight difficult. This conclusion agrees, moreover, with the remarks of Baron von Humboldt, who carefully observed the mosquitoes of Central America.

From the above experiments it is inferred that the limits of functional activity for the *C. mosquito* are: as regards temperature, between 60° and 100° F., the insect reviving, however, after having been chilled to near 32° F., or warmed to 105° F.; as regards altitude, from the level of the sea to 3000 or 4000 feet. Now the limits which most observers assign to the propagation of yellow fever are temperatures ranging from 60° F. to 90° F. ("Barton's Reports," 1852, pp. xiii. and 283); a general temperature of 32° F. having, however, proved ineffectual to prevent the recurrence of the disease (in the case of the "Plymouth"), when a tropical temperature was produced. As regards altitudes, the highest limit at which it has been observed seems to be 4000 feet above the level of the sea.

Before dismissing the subject under consideration, I must add that the mosquito finds within the precincts of a dwelling all the requirements for its development, growth, and reproduction; dark corners to hide in, stagnant water in which to lay its eggs and to develop its larvae, and substances for the female insect to feed on, being the principal conditions. A forgotten tub, or pool of stagnant water in a back yard or garden, is often chosen by the insects as a place of rendezvous where they congregate and lay

their eggs; the larvae, in the meantime, going through their successive stages of development. The mother insect when about to die, has been observed to resort to the water where its larvae are growing, its cadaver remaining floating upon the liquid surface. The nocturnal species will naturally lead a more stationary existence than the diurnal; for the latter, in trying to sting during the busy hours of the day, will often have to follow its intended victim from house to house, returning again and again after being driven off, until it succeeds in planting its sting and filling with blood. Wherever the bite happens to have been successful, there the mosquito will, in all likelihood, take up its quarters; it will develop a new brood and continue to sting all that come in its way, unless again led off by a chance peregrination.

Before relating the following six cases of experimental yellow fever, it will be proper to explain the general principles by which I was guided, and the process which I have followed in my inoculations.

The general disposition of the *C. mosquito's* sting has already been described, but for our present purpose it may be regarded as a slender (p. 402) hollow needle from $\frac{1}{30}$ to $\frac{1}{40}$ mm. broad and 2 mm. long, with its sides roughened by a series of transverse ridges and its point armed with teeth. This needle penetrates through the skin until it reaches one of the capillaries of the corium, generally to the depth of 1 to 2 mm., remains in position during a space of from one to five minutes, and, after being withdrawn, will continue protected by its sheath against external agents until the insect's next bite. I have been able to prove that the sting often retains spores of microscopical fungi, which may be made to develop by keeping the proboscis in a sterilized cell, and I once found upon the side of the sting a finely developed bunch of spores like those observed in yellow fever blood cultures by Dr. Sternberg (*Bacteria*, 2d edition, p. 426), and classified as "*Penicillium*;" whence it is to be inferred that it may likewise retain upon its outer surface or inside of its sheath, such minute disease-germs as are generally believed to occasion most of the zymotic diseases. If so, the sting of the mosquito having been impregnated with the animal juices during

the operation of stinging, may constitute an appropriate soil for the preservation or even for the culture of those germs; might it not, indeed, be the "intermediate host" necessary for some phase of their development?¹

For the purpose of carrying into effect this novel inoculation, my plan has been to catch a female mosquito while in the act of stinging and before it has filled, by inverting an empty phial or test-tube over it and closing the mouth of the phial with a plug of cotton-wool. The insect is thus in readiness to renew its bite as soon as it has become accustomed to its place of confinement. Indeed, it will die of inanition if not allowed to do so in the course of a few hours (four to twelve in summer). The captive is then taken to a confirmed case of yellow fever, and the tube being inverted and the cotton plug carefully removed over the bare surface of the patient's arm or hand, the insect is allowed to fill at leisure with the tainted blood, and the plug reinserted. After this blood has been digested, generally between the second and fourth day, the mosquito is applied in the same manner to the arm of a subject liable to the disease, and then allowed again to fill itself completely. This is the inoculation; and when successful, at the end of from five to twenty-two days incubation, the first symptoms of mild yellow fever will manifest themselves in the inoculated subject.

The process, as above described, is simple enough, but it must be observed that in order to obtain available results several conditions are necessary. A case of yellow fever must be at hand at the period most favorable for the transplantation of the virus, which, according to my (p. 403) experiments, seems to be from the third to the sixth day. A liable subject must be found willing to submit to the process, supposed to be free from previous infection, and likewise willing to keep clear from infected places during the incubation, yet within easy reach of observation.

The nocturnal species of mosquito can easily be procured, but,

¹ In resolving to experiment upon human subjects, I relied upon the inference that the quantity of virus carried by a single sting must be a minimum dose, capable of producing only the mildest forms of the disease ever observed in nature, and that a number of such bites would be necessary to occasion a dangerous attack.

as before stated, I have never succeeded in making that particular kind sting more than once; whereas, the diurnal, which is the only one that I have experimented with, does not generally come in swarms, but singly, or in small numbers, making but little noise, and its bite is usually unfelt, at least by the acclimated.

These requisites, so difficult to be obtained by one whose leisure hours, in the midst of an active professional life, are necessarily limited, will account for the small number of my experiments, some twenty-four individuals only having been inoculated by me since June, 1881. Of this number only one has died of yellow fever; he had been inoculated in November, 1883, without any visible result, and was attacked, after severe exposure, in June, 1884, with a malignant form of yellow fever (it is the second case of the series referred to elsewhere as instances of contagion). Of the remaining twenty-three, two left the country, or were lost sight of the first summer after inoculation, the rest having remained under observation during periods ranging between one and four full summers in the city of Havana. Six of these inoculations were followed within the ordinary limits of yellow fever incubation (five to twenty-two days), by an attack of fever, the exact counterpart of mild attacks of yellow fever, of which I have kept careful notes, and which were proved by subsequent observation to have conferred immunity. Eleven inoculations, though not followed by any morbid manifestation, at the end of several months a mild attack of yellow fever (without albuminuria) was observed.

These figures are not considered, from a statistical point of view, to afford any definite clue either in favor of or against the prophylactic value of my inoculations when not followed by a mild attack of the disease, and it is rather upon the circumstances attending my six successful inoculations that I rely in order to prove the aptitude of the *C. mosquito* for transmitting yellow fever. If this be once admitted, it must follow that the disease is actually so transmitted, since it must constantly happen, in a place like Havana, that unacclimated subjects (p. 404) are stung by mosquitoes which have previously bitten yellow fever patients.

My first inoculations by means of mosquitoes were performed under the following circumstances: A group of twenty unacclimated soldiers, who were quartered on the heights of the Cabanas, on the other side of the bay, were picked out for my observations, and were only allowed to cross the bay in batches of four or five on the days they were sent to my office, where I tried their blood for hematimetric purposes. Five of the group were inoculated by me at different dates between the 29th of June and the end of August, 1881. The first three were followed, at the end of five or fourteen days' incubation, by an attack of fever of several days' duration, diagnosticated by the attending physicians at the military hospital as "regular yellow fever" in the first case, and "abortive yellow fever" in the two others. The fourth inoculated soldier suffered only from continued headache, and, on the fifteenth day after the inoculation, came to my office with slight fever (temperature 100.7° F., pulse 100), but was not laid up. The fifth did not return to my office. I was informed that he had felt poorly a few days after the inoculation, but was not laid up. I have been able to trace the history of these five cases until the beginning of last year. None of them had been reported, up to that date, as subsequently attacked with yellow fever. Of the remaining fifteen soldiers of the group, upon whom the inoculation *was not performed*, none were attacked with yellow fever during the period of my observation, June 28 to September, 1881.

CASE I—On the 30th of June, 1881, one of the soldiers of the above group (F. B.), twenty-two years of age, three months in Havana, having had previously some attacks of intermittent fever, was inoculated by means of a mosquito which had bitten, two days before (June 28th), a patient in the fourth day of yellow fever and who died thirty-six hours later.

July 14. The inoculated soldier was taken sick and went to the Military Hospital, where I was only able to see him on the 16th (third day of his illness). I found him with slight fever, slight yellowish tinge of conjunctivae, pains of invasion almost disappeared; the urine gave distinct evidence of albumen with heat and with nitric acid, not having presented any in the morn-

ing. The clinical report of the attending physician, together with my own observation, gave the following result.

1st day, July 14. Invasion preceded by a few days of discomfort.

2d day. Morning: Temp. 101.8° F.; pulse 92; resp. 28; face and eyes injected; intense headache; slight epigastralgia; pains in the spine; tongue coated; no vomiting or other remarkable symptoms. Treatment: Ipecacuanha four grammes in four doses; cream of tartar lemonade; absolute diet. Evening: Temp. 100.4° F.; pulse 88; resp. 26; headache less intense. Night: Intense thirst; urine scanty.

3d day. Morning: Temp. 99.6° F.; pulse 72; resp. 34, skin pale; slight yellowness of conjunctivae; congested gums; epigastralgia; no nausea; no albumen in the urine. Evening: Albumen detected in the urine. Night: Same condition; insomnia. Treatment: One gramme of sulphate (p. 405) of quinine in ten doses; cream of tartar lemonade; mustard plasters to the extremities.

4th day. Morning: Temp. 98.9° F.; pulse 72; resp. 34; no headache; some appetite; gums give a little blood on compression; urine treated by heat and nitric acid, gives a more abundant precipitate of albumen. Evening: Normal temperature and pulse.

5th day. Temp. 98.9° F.; pulse 78; respiration normal; slight jaundice; urine contains albumen.

6th day. Convalescent; urine not examined; broth allowed.

7th day. Continues well.

12th day. Cured.

The distinct evidence of albumen in the urine, notwithstanding the mildness of the fever and general symptoms, leaves no doubt regarding the diagnosis, which was unhesitatingly reported as "regular yellow fever."

CASE II.—Another soldier of the group (A. L. C.), seventeen years of age, three months in Havana, was stung on the 22d of July, 1881, by a mosquito which had bitten, on the 16th, a bad case of yellow fever (in fifth day of his illness), and on the 20th had been made to sting my own hand.

July 27. Five days after the inoculation, this soldier entered

the Military Hospital with an attack of fever, which was qualified as "abortive yellow fever." When seen by me on the 31st (fifth day of his illness), there was scarcely any fever, and the urine contained no albumen. I was unable to procure the clinical notes of this case.

This observation would tend to prove that an infected mosquito does not always lose its virulence by an intermediate bite. This is not always the case, however, for on a subsequent occasion, having inoculated with a mosquito which had bitten two yellow fever patients, a person who seems thereby to have acquired subsequent immunity, the same insect was afterward made to sting a second non-acclimated person, who had a severe attack of yellow fever six months later, from which he fortunately recovered. This case has not been included among my regular inoculations, being considered a distinct experiment.

CASE III.—A third soldier (D. L. F.), twenty years of age, and six months in Havana, was inoculated on the 31st of July, 1881, with a mosquito which had bitten, two days before, a fatal case of yellow fever in third day of the disease. On the 5th of August (five days after the inoculation) the soldier came to my office, presenting temp. 39.6° , and pulse 110. He was at once sent to the Military Hospital, where the following clinical record was taken:

1st day, August 5. Evening: Temp. 103.2° F.; pulse 112; intense headache; slight epigastralgia; flushed countenance; intense thirst. Treatment: Valerianate of quinine two grammes in twenty pills; mustard plasters to the extremities; cold applications to the forehead.

2d day. Morning: Temp. 100.7° F.; pulse 72; resp. 28; the pains have lessened; some nausea; subicteric tint; urine pretty abundant, contains no albumen. Evening: Temp. 101.8° F.; pulse 88. Night: Temp. 100.7° F.; pulse 82; insomnia.

(p. 406) *3d day.* Morning: Temp. 99.6° F.; pulse 76; perspiration; no pains. Evening: Temp. 100° F.; pulse 80; restlessness.

4th day. Apyrexia.

The diagnosis, as stated in the clinical report, was "abortive yellow fever."

The following year (1882) my attention was principally devoted to the observation of mild forms of yellow fever, in order to collect reliable data available for the appreciation of my experimental cases. In 1883, however, I resumed my experiments, obtaining three successful inoculations, one of which (Case V.) is particularly worthy of notice.

CASE IV.—A Spaniard (J. B.), employed as a servingman to my friend Dr. Delgado, twenty-five years of age, nine months in Havana, having never been ill since his arrival, was inoculated on the 22d of June, 1883, by two mosquitoes, which had both bitten, two days before, a fatal case of yellow fever in the sixth day of his illness.

July 9th (seventeen days after the double inoculation), J. B. was taken ill with symptoms of yellow fever. The following morning an emetic was administered, followed by a dose of castor oil; no other medicine being given in the course of the illness, and absolute diet maintained until the sixth day, only water being allowed.

2d day. Morning: Temp. 101.3° F.; pulse 80; face flushed; pains in the loins. Evening: Temp. 101.8° F.

3d day. Morning: Temp. 100.4° F.; pulse 70; no albumen in the urine. Evening: Temp. 101.8° F.; face less flushed; straw color of the conjunctiva; intense thirst; anorexia.

4th day. Morning: Temp. 99.5° F.; pulse 68; no albumen. Evening: Temp. 101.3° F.; pulse 70.

5th day. Morning: Temp. 100.4° F.; pulse 68; no albumen; conjunctivae yellowish; gums do not bleed on pressure.

6th day. Morning: Temp. 101.4° F.; pulse 72. Midday: Temp. 103.1° F.; pulse 72. Evening: Temp. 103.2° F.; pulse 70.

7th day. Morning: Temp. 98° F.; pulse 54; yellowish tinge on the forehead; no pains; has perspired freely in the night; milk allowed. Evening: Temp. 98.6° F.; pulse 52; appetite returning; rapid convalescence.

The general type of the fever, with remission on the fourth day, and defervescence on the seventh, bears a strong resemblance to some forms of natural yellow fever that I have observed. The patient has since remained protected.

The following case is remarkable from the circumstance that most of the conditions were fulfilled that can well be secured in the vicinity of Havana, in order to avoid the chances of independent infection from other sources besides the inoculation. The place selected for the experiment was the same country residence or "Quinta" rented by the Jesuit Fathers since 1872, near the "Quemados de Marianao," to which Dr. Stanford E. Chaillé has alluded in his remarkable report as President of the Yellow Fever Commission which visited Havana in 1879 (*Annual Report of the National Board of Health*, Washington, 1880, p. 276 (p. 407)). In the course of eleven years (1872-1883), the only case of yellow fever developed among the many liable subjects who had spent their summer vacations at this place, during their stay, occurred in 1880 in a young priest who had been going backward and forward to Havana during the previous fortnight, and who was attacked with the disease during his last visit to the city, where he remained and died. It is more than likely that he had contracted the infection in town, and not at the Quinta.

Toward the end of June, 1883, several young priests and a servant, all unacclimated and having arrived from Spain the previous autumn, happened to be staying at this country-place, and I availed myself of their willingness to submit to my inoculation experiments.

CASE V.—P. U., one of the unacclimated priests, a young man of spare habit, having gone to the "Quinta" toward the end of June, 1883, did not again visit the city nor the neighboring town of Marianao until the following September. On the 15th of July a first unsuccessful attempt was made with a mosquito contaminated from a case in the seventh day of yellow fever; a full month was then allowed to elapse before a second attempt on the same person.

August 18, 1883, P. U. was inoculated with a mosquito which had bitten on the 13th and 16th two separate cases of yellow fever, each in the sixth day of their illness.

On the 26th of August, eight days after inoculation, P. U. was taken ill about 8 A.M. with headache, pains in the loins, and fever (temp. 100.7° F.). I saw him at 4 P. M. and from that time followed the case, keeping accurate notes of the symptoms.

1st day. 4 P. M., felt very poorly, complained of headache and pains in the loins and calves; face flushed and covered with perspiration; eyes injected; was sent to bed, and after a while presented: Temp. 102.2° F.; pulse 100, dicrotic. Treatment: Castor oil with lime juice. Night: Temp. 102.3° F.; pulse 104; vomited five or six times through the night and had several passages; thirst; eyes injected.

2d day. Morning: Temp. 101.3° F.; pulse 88; resp. 20; eyes injected, without yellow tinge; urine natural in appearance. Evening: Temp. 101.4° F.; pulse 90; resp. 30; somewhat drowsy; urine less copious than usual, acid reaction, not affected by boiling. Treatment: Hyposulphite of soda; boiled orangeade for common drink.

3d day. Morning: Temp. 101.8° F.; pulse 80; resp. 27; urine contains no albumen; restless night, insomnia; tongue white; thirst; face less flushed. Evening: Temp. 101.8° F.; pulse 84; resp. 26; subicteric tinge of conjunctivae. Same treatment.

4th day. Morning: Temp. 100.4° F.; pulse 60; resp. 27; subicteric tinge more marked; the pains have ceased; urine scanty, contains biliverdine, but no albumen; the gums bleed on pressure. Treatment: Chlorate of potash. Evening: Temp. 101.4° F.; pulse 80; restlessness; urine scanty, no albumen; thirst; anorexia.

5th day. Morning: Temp. 101.1° F.; pulse 76; resp. 29. Evening: Temp. 101.8° F.; pulse 83. Night: During a thunderstorm became very nervous; ten hours without passing urine; urine presents traces of albumen. Treatment: Morphia syrup.

(p. 408) *6th day.* Morning: Temp. 101.8° F.; pulse 72; urine not altered by ebullition; quiet night; expectorated some bloody sputa. Broth allowed. Evening: Temp. 100.7° F.; pulse 75.

7th day. Morning: Temp. 99.6° F.; pulse 62; resp. 20; subic-

teric tint of conjunctivae; some bloody sputa; gums bleed on pressure; urine scanty, no albumen. Evening: Temp. 98.9° F.; pulse 57.

8th day. Morning: Temp. 98.7° F.; pulse 58; subicteric tint of conjunctivae.

It is worthy of notice that this patient in his normal condition presented a *polyuria insipida*, amounting to over two litres per day; the secretion becoming immediately reduced from the invasion of the attack.

The patient spent two summers in the city after this attack, visiting cases of yellow fever, and having witnessed two severe ones in the town-college where he resided, without experiencing any inconvenience.

CASE VI.—The unacclimated servant before mentioned, who was staying at the Jesuits' "Quinta" with the preceding case, and upon whom a first unsuccessful attempt had also been made on the 16th of July, was again inoculated on the same day as P. U.

August 18. This servant (J. S.) was stung by a mosquito which had bitten, three days before, one of the patients of yellow fever from whom the previous case was produced. J. S. remained at the "Quinta" until September 3d, at which date he had to return to the college in town. He was taken ill on the 9th and went into a private hospital, where I was able, with Dr. Delgado's assistance, to follow up the case.

1st day. Twenty-two days after the inoculation, taken ill in the evening, with fever, headache, and pains in the loins.

2d day. Midday: Temp. 103.1° F.; pulse 94; copious perspiration; headache; pains in the loins; eyes injected; tongue coated. Evening: Temp. 103.2° F.; pulse 96; resp. 24; urine acid, not precipitated by boiling.

3d day. Afternoon: Temp. 100.4° F.; pulse 84; resp. 20; urine acid, gives a distinct precipitate on being heated to the boiling point; tongue coated; face less flushed; thirst; anorexia.

4th day. Afternoon: Temp. 99.8° F.; pulse 66; resp. 22; urine

not precipitated by heat nor by NO_2 ; subicteric tint of conjunctivae; thirst; anorexia.

5th day. Midday: Temp. 99.3°F. ; pulse 64; resp. 22; urine turbid, no albumen; appetite returning.

6th day. Afternoon: Temp. 99.8°F. ; pulse 64; resp. 22; broth allowed.

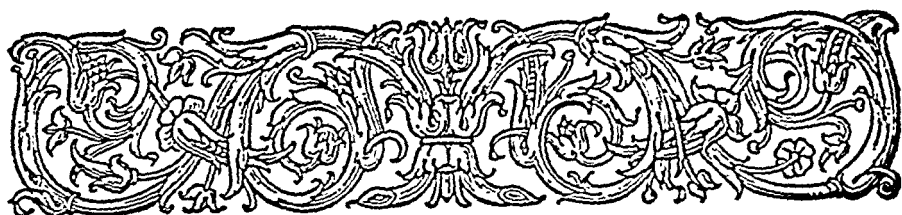
7th day. Temp. 99.3°F. ; pulse 56; resp. 22; some appetite; conjunctivae subicteric.

The fact that this person had returned to Havana six days before the attack, together with the long incubation of twenty-two days, leaves a doubt regarding the part that the inoculation may have had in the causation of the disease; but, on the other hand, the small number of yellow fever cases reported at that time in Havana, and the circumstance that newcomers are not often attacked so early as six days after (p. 409) their arrival in the city, have induced me to include this among my successful inoculations.

From the evidence adduced in the preceding pages, I conclude that while yellow fever is incapable of propagation by its own unaided efforts, it may be artificially communicated by inoculation, and only becomes epidemic when such inoculations can be verified by some external natural agent, such as the mosquito.

The history and etiology of yellow fever exclude from our consideration, as possible agents of transmission, other blood-sucking insects, such as fleas, etc., the habits and geographical distribution of which in no wise agree with the course of that disease: whereas, a careful study of the habits and natural history of the mosquito shows a remarkable agreement with the circumstances that favor or impede the transmission of yellow fever. So far as my information goes, this disease appears incapable of propagation wherever tropical mosquitoes do not or are not likely to exist, ceasing to be epidemic at the same limits of temperature and altitude which are incompatible with the functional activity of those insects; while, on the other hand, it spreads readily wherever they abound. From these considerations, taken in

connection with my successful attempts in producing experimental yellow fever by means of the mosquito's sting, it is to be inferred that these insects are the habitual agents of its transmission. It cannot be denied, however, that other such agents may and probably do occasionally occur, but not being endowed with the same facilities for rapid and extensive operation, their influence becomes insignificant as compared with the action of the Cuban culex.



Inoculations for Yellow Fever by Means of Contaminated Mosquitoes

BY

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AT THE time when my former article was written¹ I observed that the figures there given were not considered by me, "from a statistical point (p. 265) of view, to afford any definite clue either in favor or against the prophylactic value of my inoculations." In fact neither the number of my experiments nor the length of time during which the parties inoculated had been under observation could at that time justify any scientific deductions. Now, however, the case is different; I have on record a series of sixty-seven persons, including all those whom, in collaboration with Dr. Delgado, I have inoculated since 1881, by means of contaminated mosquitoes, in the manner explained in my previous article. All were Europeans, with few exceptions natives of Spain, young adults recently arrived in Cuba and presenting the usual conditions which imply liability to contract yellow fever. Among the sixty-seven a considerable number, fifty-two, are considered as acclimated, either from the fact that they have resided in the infected quarters of the city of Havana (the old town) during

¹"Yellow Fever: Its Transmission by Means of the *Culex* Mosquito." *American Journal of the Medical Sciences*, October, 1886, p. 395.

periods varying between three and seven years; or in consideration of their having experienced fevers which are attributed to the yellow fever infection, though of a mild type in the vast majority of the cases. Two parallel groups, one of thirty-three *inoculated* persons and the other of thirty-two *not inoculated*, both offering to all intents and purposes such similarity (as to susceptibility and exposure) as can seldom be obtained, afford a reliable foundation for a fair and unbiassed comparison. I consider, therefore, that the time is now come when some practical inferences may be drawn, and, as far as they go, I am happy to say that they agree with my former expectations.

The statistical method of demonstration is, at best, a tedious and a slow process, but it can boast of great triumphs, such as are recorded in the instances of Jenner and Pasteur, who have had to rely exclusively on its results in order to bring over to their views the balance of scientific opinion and public favor. They represent, moreover, two distinct applications of that method. Jenner vaccinated indiscriminately a vast number of subjects in order to verify subsequently the immunity enjoyed by the majority when exposed to the variolous infection. Pasteur, on the other hand, adopted the system of carefully registering every person inoculated by his method after being bitten by a rabid animal, the average proportion of hydrophobic cases developed in the non-inoculated after similar bites. I have chosen Pasteur's plan, believing it to be the more reliable and more applicable to our case. It cannot be denied, however, that, limited as we have been in our field of experiment, our numbers cannot compare with those of the glorious French investigator, nor that we labor under a disadvantage in having to deal with a disease which so far has not been proved to occur, under ordinary circumstances, in lower animals. Thus obliged to confine our investigations to the human species, it could hardly be expected of us that we should carry our scientific zeal to the point of seeking, through a bolder application of our inoculations, to determine a violent attack of the disease—thereby carrying conviction, no doubt, to the sceptical mind, but at the risk of having betrayed the confidence placed in us.

A somewhat specious objection was recently raised against our mosquito-inoculations, on the plea that the proboscis of the insect not being susceptible of sterilization many accidental germs might be inoculated together with or instead of yellow fever, supposing the latter to exist in the proboscis of the contaminated mosquito. To this hypothetical imputation I can oppose many facts. In none of our numerous inoculations has such an occurrence been observed, nor has it ever been proved that the acclimated inhabitants who are constantly being stung by those insects acquire thereby any specific infection. I have on several occasions introduced into sterilized tubes provided with agar jelly mosquitoes that had stung acclimated persons. In most of these experiments, after several days' confinement, the insect died for want of food, and yet not a single colony appeared upon the jelly; when any growth was developed it mostly consisted of fungi, the spores of which had probably been introduced accidentally while transferring the insect from one tube into another. From this curious result I infer that the insect has some means of rendering its outer surface aseptic, and probably does so through a very peculiar operation which I have often seen it perform. This consists in collecting with its hind or middle legs a secretion expelled from the posterior part of its body, and besmearing very persistently with it every part of its body—legs, wings, head, and proboscis. I also believe that we are justified in admitting that the liquid which the insect employs to lubricate its complicated sting, and which being poured into the wound occasions the painful sensation felt by its victim, must vary in its chemical composition in different species of gnats, thereby accounting for the difference in the sensations occasioned by their sting. It is quite possible, therefore, that the presence of that liquid may constitute in the sting of the *Culex* mosquito an appropriate soil for the development of the yellow fever germ, whereas the same germ would remain sterile in the sting of other species of *Culex*.

Another objection of a clinical character was made to our considering as cases of mild yellow fever the attacks of non-albuminuric fever observed in our inoculated subjects, either within the

plausible limits of incubation or later on, with the result of rendering them immune against subsequent attacks of albuminuric yellow fever. To this objection an answer is given by the present statistics themselves, inasmuch as among fifty-six inoculated and non-inoculated subjects mentioned therein and who have resided during periods varying between three and seven consecutive years in the city of Havana, *one-half* have acquired their immunity exclusively through non-albuminuric attacks suffered during the first three years after their arrival here. If the objection turned out to be well grounded, it would only prove that what we had considered as a partial immunity had been a complete one in ninety per cent. of our inoculated subjects.

I have distributed our sixty-seven inoculated subjects into six groups:

GROUP I. Fifteen—whose observation is yet incomplete, not having resided three years in Havana, nor experienced any form of yellow fever.

GROUP II. Twelve—who experienced, within a period of days' varying between three and twenty-five, after the inoculation, an attack of fever with or without albuminuria.

GROUP III. Twelve—who did *not* experience any pathogenic effects within the twenty-five days following the inoculation, nor any other febrile attack subsequently, that could be referred to the yellow fever infection.

GROUP IV. Twenty-four—who did not experience pathogenic effects within the twenty-five days, but subsequently had fevers of a mild type, either non-albuminuric or with slight or transient albuminuria.

GROUP V. Three—who experienced no pathogenic effects after the inoculation, but were subsequently attacked with regular albuminuric yellow fever (severe in two cases), but recovered.

GROUP VI. One—who not having experienced pathogenic effects after the inoculation, was attacked some months later, and after exposure to an infection of unusual intensity, with fatal yellow fever.

After excluding the fifteen incomplete observations of Group I.,

fifty-two cases remain to be considered which may be conveniently arranged under three heads:

	Cases	Per cent
Mild acclimation (Groups II., III., IV.).....	48	92.2
Acclimation with regular yellow fever—cured.....	3	5.9
Fatal yellow fever.....	1	1.9
	<hr/> 52	

The next point was to obtain reliable data for comparison. I was fortunate in receiving from two religious communities placed under my medical charge the authorization to practise my inoculations on such members as would be willing to submit to them. These communities are those of the Jesuit and Carmelite Fathers, established in the city of Havana. Their members are partially renewed almost every year by the arrival of new-comers from Spain to substitute others who have resided several years here. Since 1883, every year except 1885 I have inoculated some of the new-comers, while others did not go through that ordeal. During the period 1883–1890 the Jesuit Fathers have had thirty-six inoculated and seven not, and the Carmelites had thirteen inoculated and twenty-five not inoculated. Of the inoculated none have died of yellow fever, whereas five of the non-inoculated have died of it (one Jesuit and four Carmelites). After deducting from the inoculated thirteen cases still under observation, we have thirty-three inoculated and thirty-three not inoculated members of the same communities, having arrived in the same years as the former, leading the same life and exposed to the same chances of infection.

	Inoculated Per cent	Not inoculated Per cent
Mild acclimation (Groups II., III., IV.)	31-94	21-65½
Acclimation with regular yellow fever—cured.....	2-6	6-19
Died of yellow fever—none of the inoculated, but of the non-inoculated.....		5-15½
	<hr/> 33	<hr/> 32

The conclusions which the above statistical results, together with the comparative observations, appear to justify are as follows:

1. The inoculations with one or two recently contaminated mosquitoes, in the manner practised by ourselves, is free from danger, inasmuch as the numerous trials which have been made have produced at most (in about 18 per cent. of our cases) a mild attack followed by immunity.

2. We must attribute to the influence of the inoculations with contaminated mosquitoes: 1. The mild acclimation observed in 94 per cent. of our cases, whereas the same desirable result has only occurred, *caeteris paribus*, in $65\frac{1}{2}$ per cent. of the non-inoculated; 2. The reduction of cases of regular yellow fever to the proportion of 6 per cent. instead of 19 per cent.; and 3. That of fatal yellow fever to less than 2 per cent. instead of $15\frac{1}{2}$ per cent., one single death from yellow fever having occurred among the sixty-seven persons inoculated by us since 1881 until the present date.

3. The contaminated mosquitoes appear to lose either partially or completely their contamination after they have stung healthy subjects; whereas the contamination appears to become intensified by successive stings of the same insect on yellow fever patients.

4. The inoculations performed during the colder season should not be considered to afford sufficient protection, but should be repeated on the approach of the hot season.

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EPHRAIM McDOWELL

[1771-1830]

MEDICAL CLASSICS

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Ephraim McDowell

BIOGRAPHY

- 1771 Born November 11 in Rockbridge County, West Virginia, the ninth of twelve children. He was of Scottish and Irish ancestry. His father, Samuel McDowell, was a member of the legislature of Virginia until he was appointed a judge and a land commissioner for Kentucky.
- 1783 Age 12. Family moved to Kentucky where Ephraim attended the classical seminary of Messrs. Worley and James at Georgetown, Kentucky.
- 1790 Age 19. Studied medicine with Dr. Humphreys of Staunton, Virginia.
- 1793 Age 22. Went to Edinburgh to study medicine under John Bell and Alexander Monro, Secundus, among others; did not receive a degree.
- 1795 Age 24. Returned to practice in Danville, Kentucky.
- 1800 Age 29. Sponsored a library in Danville.
- 1802 Age 31. Married Sarah Shelby, daughter of the first governor of Kentucky, General Isaac Shelby, and had eight children.
- 1807 Age 36. Given a diploma by the Medical Society of Philadelphia.
- 1809 Age 38. Performed first ovariectomy in history, on Jane Todd Crawford.
- 1812 Age 41. Operated on James K. Polk (later President), a youngster of seventeen, for urinary calculus.
- 1817 Age 46. Published first paper on ovariectomy. *Three cases of extirpation of diseased ovaria.*

- 1822 Age 51. Traveled several hundred miles to Hermitage, Tennessee, where he removed an ovarian tumor from the wife of a close friend of Andrew Jackson, who himself assisted with the operation. McDowell asked \$500.00 for a fee, but received \$1500.00.
- 1825 Age 54. Given the degree of Doctor of Medicine by the University of Maryland.
- 1830 Age 69. Died June 20, after a brief illness, possibly of a gangrenous appendicitis.

One of the founders and a member of the first board of trustees of Center College at Danville, Kentucky.

- 1879 The Kentucky State Medical Society erected a monument over McDowell's grave in McDowell Park, in Danville.

WRITINGS

1. Three cases of extirpation of diseased ovaria. *The Eclectic Repertory and Analytical Review, Medical and Philosophical*, 7: 242-244, 1817.
2. Observations on diseased ovaria. *Ibid.*, 9: 546-553, 1819.

BIBLIOGRAPHY OF BIOGRAPHIES

- Biography in *Lives of eminent American physicians and surgeons*. By S. D. Gross. Philadelphia, Lindsey and Blakiston, 1861. 8°, pp. 207-230.
- Interesting incidents in the private life of Ephraim McDowell. By J. P. Chesney. *Cincin. Med. Report*. 3: 133-136, 1870.
- Biographical sketch. By J. D. Jackson. *Richmond and Louisville Med. Jour.*, 16: 642-650, 1873.
- The first ovariectomy. A letter. By J. D. Jackson. *Brit. Med. Jour.*, 1: 467, 1874.
- Memoir by J. H. Letcher. *Tr. McDowell Med. Soc., Evansville, Ind.*, pp. 36-63, 1875.
- Necrology. By L. S. McMurtry. *Tr. Amer. Med. Ass.*, 29: 708-712, 1878.

- Memorial oration in Danville, Ky., May 16, 1879, in honor of Ephraim McDowell, "The father of ovariectomy." By S. D. Gross. Louisville, Morton, 1879. 8°, 77 pp. Also, abstr.: *Med. Record*, 15: 499-500, 1879.
- Dedication of the monument to Ephraim McDowell. *Cincin. Lancet and Clinic*, n.s. 2: 401-412, 1879.
- The biography of Ephraim McDowell—; together with valuable scientific treatises and articles relating to ovariectomy, and eulogistic letters from eminent members of the medical profession in Europe and America. By Mary Y. Ridenbaugh. New York, C. L. Webster and Co., 1890. xvi, 558 pp., 3 pl., 22.5 cm. Same, 2 ed., rev. Philadelphia, the author, 1894. xvi, 624 pp., 19 port., 2 pl., 21.5 cm. Same, rev. ed. New York, McDowell Pub. Co., 1897. xvi, 558 pp., 3 pl., 22.5 cm.
- Memorial address by L. S. McMurtry. *Tr. South. Surg. and Gynec. Ass.*, 1893, 6: 22-36, 1894. Also: *Med. News*, 64: 179-183, 1894.
- Response to the toast, "Ephraim McDowell." By J. Eastman. *Jour. Amer. Med. Ass.*, 25: 882-883, 1895.
- Heroes of medicine. *Practitioner*, 58: 53-56, 1897.
- Biography by J. H. Letcher. *Amer. Pract. and News*, 32: 6-8, 1901.
- Biography by W. L. Lowder. *Med. and Surg. Monitor*, 4: 109-112, 1901.
- Biographical sketch. *Columbus Med. Jour.*, 26: 586-590, 1902.
- The passing of the historic McDowell building at Danville, Ky. By W. L. Lowder. *Physicians and Surgeons*, 24: 241-258, 1902.
- McDowell, the father of ovariectomy. By J. R. Goffe. *Amer. Jour. Obst.*, 59: 737-752, 1909. Also: *Surg., Gynec. and Obst.*, 8: 449-458, 1909.
- A sequel to McDowell's triumph, being a brief sketch of the rise and progress of the Samaritan Free Hospital. By A. H. G. Doran. *Amer. Jour. Obst.*, 59: 752-758, 1909.
- Biography by L. S. McMurtry. *New York Med. Jour.*, 89: 933-936, 1909.

- Ephraim McDowell in 1809. By S. M. Brickner. Tr. Amer. Gynec. Soc. 34: 589-591, 1909.
- The McDowell centenary celebration. By S. C. Swartsel (et al.). *Lancet-Clinic, Cincinnati*, 102: 681-693, 1909.
- Obituary by F. C. Warnshuis. *Jour. Michigan Med. Soc.*, 8: 586-589, 1909.
- Das Centennarium der Ovariectomie. By A. Martin. *Monatsch. f. Geburtsch. u. Gynäk.*, 30: 675-696, 1909.
- McDowell: the father of abdominal surgery. By G. Gellhorn. *Interstate Med. Jour.*, 17: 600-608, 1910.
- Biography by S. C. Swartsel. *Eclect. Med. Gleaner, Cincinnati*, n. s. 6: 97-106, 1910.
- The indebtedness of posterity to the pioneer surgeon of the Mississippi valley. By J. D. Bryant. *Louisville Month. Jour. Med. and Surg.*, 18: 168-179, 1911.
- Some facts not generally known regarding Ephraim McDowell. By A. H. Barkley. *Surg., Gynec. and Obst.*, 15: 496-503, 1912.
- Biography by A. Schachner. *Johns Hopkins Hosp. Bull.*, 24: 153-159, 1913.
- Ephraim McDowell; the ovariectomist. By G. Foy. *Med. Press and Circ.*, n.s., 102: 495, 1916.
- Biographical sketch of McDowell. By J. D. Jackson. *Kentucky Med. Jour.*, 15: 11-17, 1917.
- Dedicatory address (at unveiling of monument to Ephraim McDowell). By S. D. Gross. *Ibid.*, 15: 26-41, 1917.
- Presentation address made in presenting Dr. McDowell's door-knocker to Dr. Gross. By R. O. Cowling. *Ibid.*, 15: 41, 1917.
- Address of Prof. Lewis A. Sayre at dedication of monument. *Ibid.*, 15: 43, 1917.
- Biography by L. S. McMurtry. *Ibid.*, 15: 46, 1917.
- Ephraim McDowell and J. Marion Sims, the American founders of gynecology. *U. S. Nav. Med. Bull.*, 14: 373, 1920.
- Biography in *Amer. Med. Biographies*. (Kelly and Burrage) 1920.
- Ephraim McDowell, "Father of ovariectomy and founder of ab-

- dominal surgery," with an appendix on Jane Todd Crawford. By A. Schachner. Philadelphia, Lippincott, 1921. 8°, xviii, 331 pp. Also, review by L. S. McMurtry. Surg., Gynec. and Obst., 34: 696-697, 1922.
- Some McDowell items. By J. Ruhräh. Med. Record, 101: 397, 1922.
- Short sketch of Dr. McDowell by O. Clark. Brazil-medico, 36: 305, 1922.
- Master surgeons of America; Ephraim McDowell. By L. S. McMurtry. Surg., Gynec. and Obst., 36: 286-289, 1923. Biography. Med. Jour. and Record, 123: 119-121, 1926.
- Biography by W. P. Rhudy. Clifton Med. Bull., Clifton Springs, 12: 91-98, 1926.
- Ephraim McDowell and ovariectomy. By I. S. Cutter. Internat. Abstract Surg., 47: 87-89, 1928.
- Address at unveiling exercises of statues of Dr. Ephraim McDowell and Henry Clay. By R. Gilbert. Kentucky Med. Jour., 27: 139-141, 1929.
- Tribute to a southern physician, Ephraim McDowell. By T. W. Moore. South. Med. Jour., 23: 1-6, 1930.
- Ephraim McDowell (with his account of first operation for removal of ovarian tumor). By E. Jelks. Jour. Florida Med. Assoc., 16: 301-303, 1930.
- Ephraim McDowell, the surgeon. By E. C. Cutler. New England J. Med., 202: 276-278, 1930.
- McDowell, pioneer and physician. By W. G. Morgan. South. Med. Jour., 24: 39-41, 1931.
- Ephraim McDowell (with account of his operations for ovarian cysts). By L. E. Burch. Ibid., 24: 36-39, 1931.
- Biography by F. J. Underwood. Ibid., 24: 41-42, 1931.
- McDowell; matured product of his labor. By G. A. Hendon. Kentucky Med. Jour., 29: 3-8, 1931.
- Jane Todd Crawford; the model patient. By Mrs. P. E. Blackerby. Ibid., 29: 8-10, 1931.
- Ephraim McDowell and early American surgery. By K. L. Sicherman. Jour. Michigan Med. Soc., 30: 453-459, 1931.

- American physicians: Ephraim McDowell. Amer. Jour. Surg., 15: 556, 1932.
- "Lest we forget." By L. Frank. Ibid., 20: 160-166, 1933.
- Surgeon of the wilderness. By W. D. Haggard. Surg., Gynec. and Obst., 58: 415-419, 1934.
- Jane Todd Crawford memorial Service. Kentucky Med. Jour. (suppl.), 33: 3-36, 1935.
- First ovariectomy performed by McDowell on Jane Todd Crawford. By R. H. Jaffé. Wien. med Woch., 85: 1357-1358, 1935.
- Biography by E. Podolsky. South. Surgeon, 5: 42-49, 1936.
- Biography in Doctors on Horseback. By J. F. Flexner. New York, Viking, 1937. pp. 121-162.
- Ephraim McDowell and Jane Crawford. By G. A. Hendon. Mississippi Doctor, 14: 14-20, 1937.

INTRODUCTION

Ephraim McDowell performed the first ovariectomy in 1809 but he did not publish his experience until eight years later. In the meantime, in 1813 and again in 1816, he had performed the operation a second and third time. Let us consider the several factors which caused the delay in announcing this operation to the world.

Ephraim McDowell was born in the backwoods of America in 1771. After studying medicine with a practitioner in Virginia for a short time, he went in 1793, at the age of twenty-two, to Edinburgh for a formal medical course. There he came under the influence of Alexander Munro, second, the anatomist, and John Bell, the anatomist, surgeon and brother of Charles Bell. In medical school McDowell was of course taught facts which were believed in his day to be true. One of these beliefs held it to be fatal to open a cavity of the body, especially the abdominal cavity. No one recognized the relation between infection and surgery in the abdominal cavity; it was seventy-four years before Lister's work on antiseptics. These dangers McDowell knew, but he was also doubtless acquainted with the spaying of animals and he may have known of the work of Houstoun of Edinburgh who had tapped an ovarian cyst in 1701.

McDowell returned to America after two years of study in Edinburgh and started practice in Danville, Kentucky. He became the leading surgeon in that part of the country and traveled hundreds of miles on horseback to attend his patients. But it was not until fourteen years later, when he was thirty-eight years of age, that McDowell's greatest opportunity came to him. He then was called in consultation to see Mrs. Jane Todd Crawford whom McDowell declared was suffering from an enormous ovarian cyst although her two local doctors believed she was pregnant. Mrs. Crawford could probably live only a year or two. McDowell determined to give her the one chance of life and health by removing the ovarian cyst. The facts were placed squarely before the patient and she chose to accept the chance of surgical intervention. McDowell insisted that the patient come to his home in Danville sixty miles away where he could operate on her in the best possible surroundings, with the best possible help and where she would remain under his own supervision.

The story of this famous operation has been told dozens of times, frequently and recently in a dramatic manner. (Read James Thomas Flexner: *Doctors on Horseback*, New York, Viking Press, 1937, pp. 121-162.) For our account we refer the reader to Mc-

Dowell's own report of the operation which is reproduced in its entirety on the following pages. The operation was a complete success. Mrs. Crawford lived thirty-one years longer and died at the age of seventy-eight.

One successful operation was not enough. McDowell waited until he had performed the operation for ovarian cyst three times. He then decided to submit his results to the medical profession. One copy of the paper which he wrote was sent to his old teacher, John Bell, in Edinburgh. Bell was ill in Italy and never saw the report. Another copy was sent to Dr. Philip Syng Physick, "the father of American surgery," who refused to have anything to do with what he thought such an obvious impossibility. McDowell then sent a copy of his paper to Dr. Thomas C. James, Professor of Midwifery at the University of Pennsylvania. This is the paper which reached publication and is to be seen on the following pages.

Most doctors refused to give any consideration to McDowell's report. Others criticized it severely because they thought it contained too little information on the physical findings, pathologic specimens and operative technique. Nearly everyone thought McDowell's experience too fantastic.

Two years later McDowell wrote a second paper in which he was able to report two additional cases of operation for diseased ovaria.

John Bell's pupil, John Lizars, used McDowell's paper in publishing his own observations on *Extraction of diseased ovaria* in 1825, without giving McDowell any credit. In the meantime, in 1821, Dr. Nathan Smith had performed an ovariectomy in Vermont without knowing anything of McDowell's work.

The brothers, Doctors John L. and Washington L. Atlee, of Pennsylvania, recognized the value of McDowell's contribution and were early champions of his operation. Many years later Charles Clay and Sir Spencer Welles of England as well as Auguste Nélaton and Jules Péan of France performed the operation and advocated it with enthusiasm.

McDowell's operation opened the way for all modern surgery of the abdominal cavity. His teaching showed that an operation within the abdomen was not necessarily fatal and from his experience there slowly began the modern surgery on all intra-abdominal organs.

Ironically, McDowell himself probably died of a gangrenous appendicitis.



Three Cases of Extirpation of Diseased Ovaria

BY

EPHRAIM M'DOWELL, M.D.

Danville, Kentucky

Published in *The Eclectic Repository, and Analytical Review, Medical and Philosophical*,
Philadelphia, 1817, Vol. VII

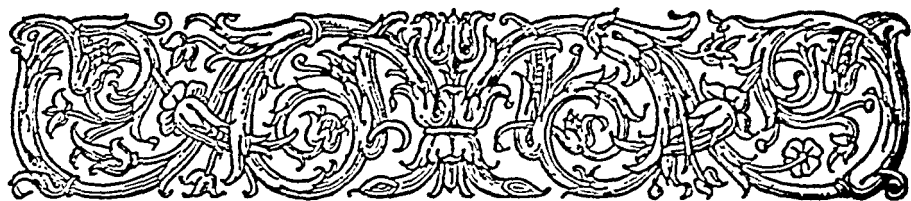
IN DECEMBER 1809, I was called to see a Mrs. Crawford, who had for several months thought herself pregnant. She was affected with pains similar to labour pains, from which she could find no relief. So strong was the presumption of her being in the last stage of pregnancy, that two physicians, who were consulted on her case, requested my aid in delivering her. The abdomen was considerably enlarged, and had the appearance of pregnancy, though the inclination of the tumor was to one side, admitting of an easy removal to the other. Upon examination, per vaginam, I found nothing in the uterus; which induced the conclusion that it must be an enlarged ovarium. Having never seen so large a substance extracted, nor heard of an attempt, or success attending any operation, such as this required, I gave to the unhappy woman information of her dangerous situation. She appeared willing to undergo an experiment, which I promised to perform if she would come to Danville, (the town where I live) a distance of sixty miles from her place of residence. This appeared almost impracticable by any, even the most favourable conveyance, though she performed the journey in a few days on horseback.

With the assistance of my nephew and colleague, James M'Dowell, M.D., I commenced the operation, which was concluded as follows: Having placed her on a table of the ordinary height, on her back, and removed all her dressing which might in any way impede the operation, I made an incision about three inches from the musculus rectus abdominis, on the left side, continuing the same nine inches in length, parallel with the fibres of the above named muscle, extending (p. 243) into the cavity of the abdomen, the parietes of which were a good deal contused, which we ascribed to the resting of the tumor on the horn of the saddle during her journey. The tumor then appeared full in view, but was so large that we could not take it away entire. We put a strong ligature around the fallopian tube near to the uterus; we then cut open the tumor, which was the ovarium and fimbrious part of the fallopian tube very much enlarged. We took out fifteen pounds of a dirty, gelatinous looking substance. After which we cut through the fallopian tube, and extracted the sack, which weighed seven pounds and one half. As soon as the external opening was made, the intestines rushed out upon the table; and so completely was the abdomen filled by the tumor, that they could not be replaced during the operation, which was terminated in about twenty-five minutes. We then turned her upon her left side, so as to permit the blood to escape; after which, we closed the external opening with the interrupted suture, leaving out, at the lower end of the incision, the ligature which surrounded the fallopian tube. Between every two stitches we put a strip of adhesive plaster, which, by keeping the parts in contact, hastened the healing of the incision. We then applied the usual dressings, put her to bed, and prescribed a strict observance of the antiphlogistic regimen. In five days I visited her, and much to my astonishment found her engaged in making up her bed. I gave her particular caution for the future; and in twenty-five days, she returned home as she came, in good health, which she continues to enjoy.

Since the above case, I was called to a negro woman, who had a hard and very painful tumor in the abdomen. I gave her mercury for three or four months with some abatement of pain; but she was still unable to perform her usual duties. As the tumor

was fixed and immovable, I did not advise an operation; though from the earnest solicitation of her master, and her own distressful condition, I agreed to the experiment. I had her placed upon a table, laid her side open as in the above case; put my hand in, found the ovarium very much enlarged, painful to the touch, and firmly adhering to the vesica urinaria and fundus uteri. To extract I thought would be instantly fatal; but by way of experiment I plunged the scalpel into (p. 244) the diseased part. Such gelatinous substance as in the above case, with a profusion of blood, rushed to the external opening, and I conveyed it off by placing my hand under the tumor, and suffering the discharge to take place over it. Notwithstanding my great care, a quart or more of blood escaped into the abdomen. After the hemorrhage ceased, I took out as clearly as possible the blood, in which the bowels were completely enveloped. Though I considered the case as nearly hopeless, I advised the same dressings, and the same regimen as in the above case. She has entirely recovered from all pain, and pursues her ordinary occupations.

In May 1816, a negro woman was brought to me from a distance. I found the ovarium much enlarged, and as it could be easily moved from side to side, I advised the extraction of it. As it adhered to the left side, I changed my place of opening to the linea alba. I began the incision, in company with my partner and colleague Dr. William Coffey, an inch below the umbilicus, and extended it to within an inch of the os pubis. I then put a ligature around the fallopian tube and endeavored to turn out the tumor, but could not. I then cut to the right of the umbilicus, and above it two inches, turned out a scirrhus ovary, (weighing six pounds) and cut it off close to the ligature, put round the fallopian tube. I then closed the external opening, as in the former cases; and she complaining of cold and chilliness, I put her to bed prior to dressing her—then gave her a wine glass full of cherry bounce, and thirty drops of laudanum, which soon restoring her warmth, she was dressed as usual. She was well in two weeks, though the ligature could not be released for five weeks; at the end of which time the cord was taken away; and she now, without complaint, officiates in the laborious occupation of cook to a large family.



Observations on Diseased Ovaria

BY

EPHRAIM M'DOWELL, M.D.

Published in *The Eclectic Repertory and Analytical Review, Medical and Philosophical*, Philadelphia, 1819, Vol. IX

Sept. 1819.

DEAR SIR, I am induced to make this statement, principally, in consequence of the observations of Dr. Henderson, which appeared in a number of the Repertory, published twelve or fifteen months since; on ovarian disease, and abdominal steatoma.

Since my former communication, I have twice performed the operation of excision; which cases are subjoined.

I shall in the first place take some notice of the remarks of Dr. Michener, which Dr. Henderson in his dissertation has thought worthy of notice. The number of the Repertory, containing the above mentioned remarks, I have unfortunately lost; but believe that I remember most of his principal strictures. In the first case related by me, in Vol. VII. the Doctor appears to take exception to the length of the incision, by pointing out the sentence which stands thus; "I made an incision about three inches from the musculus rectus abdominis on the left side, continuing the same about nine (p. 547) inches in length." As I did not actually measure the incision, it would, perhaps, have been better to have said, an incision was made, about three inches to the left of the musculus rectus, extending from the margin of the ribs to the os pubis, on a woman whose abdomen was distended by a tumour, to an enormous size. He likewise objects to the parietes of the

abdomen being contused, in consequence of the tumour resting on the horn of the saddle, during the patient's journey to Danville. Observing that the "horn of the saddle is on the right side, and the tumour was on the left." Now, with all due deference to the Doctor's knowledge in surgery, and the structure of *side saddles*, I think it would not be difficult to conceive, that a tumour weighing upwards of twenty pounds, would fill the whole abdomen, and although attached to the left ovary, the weight and bulk must have been almost, if not quite as great, on the right side as on the left. I would observe, that my patient was a woman of small stature; her abdomen had become so pendulous, as to reach almost to her knees; the size of the tumor was ascertained from actual weight. Had the left side of the abdomen been contused, I would either have delayed the operation until the contusion was removed, or operated on some other part. I never have been of opinion, that bruised flesh would heal so readily as sound; which matter I esteem of essential importance to success in this operation. The Doctor also objects to another assertion in this case, viz: "When I visited her on the fifth day, I found her engaged in making up her bed." The Doctor's scepticism, alone, appears to have carried him through the statement, and I am surprised that he will even admit the fact of her returning home, in five and twenty days after the operation, on horseback; a distance of seventy miles, and in the depth of winter.

Dr. Henderson thinks I was entirely too inconsiderate in my detail of the cases of diseased ovaria; I thought my statement sufficiently explicit to warrant any surgeon's performing the operation when necessary, without hazarding the odium of making an experiment; and I think my description of the mode of operating, and of the anatomy of the parts concerned, clear enough, to enable any good anatomist, possessing the (p. 548) judgment requisite for a surgeon, to operate with safety. I hope no operator, of any other description, may ever attempt it. It is my most ardent wish, that this operation may remain, to the mechanical surgeon, for every incomprehensible. Such have been the *bane* of the science; intruding themselves into the ranks of

the profession, with no other qualification but boldness in undertaking, ignorance of their responsibility, and indifference to the lives of their patients; proceeding according to the special dictates of some author, as mechanical as themselves, they cut and tear with fearless indifference, utterly incapable of exercising any judgment of their own cases of emergency; and sometimes, without possessing even the slightest knowledge of the anatomy of the parts concerned.

The preposterous and impious attempts of such pretenders, can seldom fail to prove destructive to the patient, and disgraceful to the science. It is by such this noble science has been degraded in the minds of many, to the rank of an art.

No case of diseased ovaria has come under my observation, similar to the one described by Dr. Henderson. The tumours extracted by myself, I have kept by me, in a state of preservation; they have been submitted to the inspection of most, if not all the physicians who have visited me. Their opinions, as to the nature of the disease, have all accorded with my own. In our most scrupulous examinations, we were never able to discover any portion of the tumours to be of a natural or healthy structure; the whole exhibition was that of a morbid undistinguishable mass, which myself and others of the faculty, who were present at the operations, were of opinion, had once been the natural ovaria; in as much as no ovarium remained on the side from whence the tumour was extracted. This was as clearly evident as it could have been on dissection after death; my incisions were made so free and extensive, that I have always performed every part of this operation by sight.

Such ovaria as I have described as dropsical, contained a gelatinous fluid in a sac about half an inch in thickness, and of a spongy texture; such as I have denominated schirrus, were of a spongy texture throughout, and somewhat elastic. Those affected with schirrus, complained of lancinating pains in the parts affected; which, from their description, were similar (p. 549) to the pains in other schirrous glands. The dropsical ovaria, are attended with a dull pain, and produce a most oppressive sense of weight in the abdomen. By these symptoms, and by a nice sense

of touch, the species may generally be distinguished from one another. How to distinguish them from steatoma and other affections which those organs are liable to, I shall not pretend to define, nor, in the present state of knowledge, do I think it at all necessary; nor even the distinction from one another.

Excision I esteem less perilous than any other mode of treatment; and the only certain cure for either of them. For schirrus and steatoma, no other relief, within our knowledge, is practicable.

The dropsical ovaria may be relieved by tapping with a large trocar. But the relief is only temporary, and would be attended with no inconsiderable danger. Some further reasons for my aversion to the trocar, I will relate hereafter.

The second case in which I operated for diseased ovaria, was the case of a negro woman in this neighbourhood. On exposing the tumour (as related in the Repertory, Vol. VII.) it adhered so firmly to the neighbouring parts, that I did not attempt its extraction, but made a free incision into it with the scalpel, and discharged its contents; she recovered of the operation, and I thought her well of the disease; but, she informed me some short time since, that it had been growing for the last twelve or eighteen months, and says it is now, about the size it was when I opened her six years ago.

None of my patients have been able to give me any satisfactory account as to the origin of the disease; with some it commenced some months after delivery. The first supposed herself pregnant, and went on to make the necessary preparation for her lying-in; the time for her delivery being protracted to a great length, and her anxiety and doubts increasing, I was called in, and immediately, on examination, per vaginam, found she was not with child.

CASE I

In April, 1817, I operated on a negro woman from Garard county; extracting a schirrous ovary, weighing five pounds. (p. 550) The incision was made near the linea alba; as in cases formerly related, I tied a cord firmly round the ligament attach-

ing it to the uterus, and cut away the ovarium; but owing to the shortness and sponginess of the part, the cord clipped off, before I laid the ovarium out of my hands, and a profuse discharge of blood took place. I immediately drew the uterus to the external incision, and commenced tying up the bleeding mouths separately. This also, in consequence of the diseased state of the parts, proved only of partial efficacy, as several of the ligatures cut through, on tying them. I now thought it all over with my poor patient, but arming a needle with a strong ligature, I passed it round the ligaments; securing it in its place by taking several stitches over its surface as I passed it round, and firmly tied it. By turning her nearly on her stomach, I was able to get most of the blood out of the abdomen, using my hand to extract the coagulated portion. The incision was then closed by the interrupted suture, and strips of adhesive plaster. She recovered happily; but, I am told her health is not good; the account I had of her was awkwardly given; from what I could learn, her complaint is hysterical. This, though the smallest ovarium I have ever extracted, was much more troublesome to the patient, than in any previous case. Besides experiencing severe lancinating pains in the parts, she was seldom able to discharge her urine, without getting almost on her head, in consequence of the tumour falling down into the pelvis, and compressing the urethra.

CASE II

A negro woman from Lincoln county, was brought to me in April, 1818, supposed, by the different physicians who had attended her, to be affected with ascites; she had been under their care about eighteen months. On examining her, I could very plainly discover the fluctuation of fluid in the abdomen, and for some months administered medicines for ascites, without effect; despairing of the power of medicines, I at length tapped her, and discharged thirteen quarts of gelatinous fluid, such as I had before met with in dropsical ovaria, of so thick a consistence, that I found it extremely difficult and tedious to discharge it. In two months after, I found it necessary to tap (p. 551) again;

during the process of discharging it a second time, the opening was frequently stopped by viscid portions of the jelly, which were broken by introducing a probe; when the abdomen was pretty well evacuated, I discovered, with the probe, a firm substance, which, on minute examination, I found to be of considerable size. I at once supposed the existence of a dropsical ovarium, in which I was confirmed, on finding the uterus empty by examination per vaginam. Some months after she was again tapped; at which time, I made the opening large enough to admit my finger; by which means, I was able to ascertain the nature of the disease beyond a doubt. I informed her master what was certainly her situation, and that nothing but excision could affect a cure. My advice was not immediately followed, nor until after she was tapped a fourth time; a week or two after which, she was brought to Danville, to undergo the operation, which was performed May 11, 1819. The diseased ovarium being on the left side, and evidently dropsical; the incision was of course made on the left side. On exposing the tumour, it was found to adhere to the parietes of the abdomen; and to the intestines, by slender cords which were easily separated with the hand, and which caused a slight effusion of blood. To the uterus, two strong ligaments adhered; one, the natural ligament, attaching the ovarium to the uterus, the other, an artificial one, attached to the fundus uteri: which appeared to be composed of the above mentioned slender cords, compacted together. I then tied fine cords of silk firmly round each of these ligaments, discharged the contents of the tumour, and cut it away.

There were sixteen quarts of gelatinous fluid discharged from the tumour and abdomen. The dressings and precautions were the same as in other cases. The second day after the operations, she was affected with violent pain in the abdomen; together with an obstinate vomiting. She was blooded as copiously as her strength would allow, but without producing any abatement of the pain or vomiting. On the third day she died. On examination after death, the uterus, contrary to expectation, appeared natural and uninflamed, the right ovarium healthy, the

silken cords were securely, and properly fixed, and not in a situation likely to injure the adjoining parts. Her (p. 552) death had proceeded from peritoneal inflammation. This membrane, throughout its whole extent, appeared greatly inflamed, and the intestines largely inflated.

I was assisted in this operation by my nephew, Dr. William A. M'Dowell. Doctors Weizegar, Tomlinson, and Horr were present.

On examining the substances we had removed, the contents of the sac presented a variety; different portions of the fluid were of different colours: semitransparent, white, brown, and yellow. There was also contained in the sac, a considerable quantity of hair; which grew from the inner surface. Enveloped in the inner substances of the sac, we found a bone, resembling, very much, in shape, the front tooth of a cow.

From the circumstance of the hair and bone, one or two of the physicians present, were inclined to believe the disease originated from an extra uterine conception; and that all of the fœtus had been absorbed, save the hair, and single bone, which was found. This question I submit to the faculty. As for myself, I think it as reasonable to suppose, the hair and bone in this unnatural situation, was the result of a morbid action. She had been delivered of a child two years before the operation, her health during that time was never good, but she had no reason to believe herself pregnant; and if it were the case, I doubt whether a whole fœtus could be so nearly absorbed in two years. There was likewise a round hole in the sac, which, from the levelled appearance of its edges, appeared of long standing; the hole was about the size of a musket ball. And there is no doubt, that the gelatinous fluid escaped through this aperture into the abdomen. This ovarium, when brought into view, was of a large size; which is the more remarkable, when we consider the enormous quantity of fluid which had been drawn off at different times, by the operation of paracentesis abdominis. During the evacuation, a bandage was kept bound tightly round the abdomen; and considerable pressure was made with the hands, in order to evacuate its whole

contents. In an attempt to draw off the contents of such a tumour with the trocar, it would be impossible to perforate all the vesicles;* and such only, as were (p. 553) pierced, would discharge their contents. While one portion of the vesicles of the ovaria would discharge themselves into the abdomen, another portion would remain diseased in the original way. Thus compounding in the system, two of the most deplorable diseases to which it is liable.

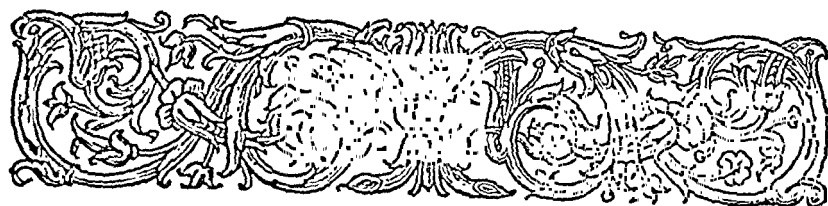
EPHRAIM M'DOWELL.

DR. JAMES.

* That this is the structure of diseased ovaria, I infer, both from authorities, and from the difficulty in discharging their contents. I have always been under the necessity of introducing my hand, and raking it forth; the obstacle to the discharge being always a membranous structure.



JAMES MARION SIMS



James Marion Sims

BIOGRAPHY

- 1813 Born Jan. 25, in the Hanging Rock Creek Section of Lancaster County, South Carolina.
- 1832 Age 19. Was graduated as Bachelor of Arts from College of South Carolina. Began study of medicine in office of Dr. G. Churchill Jones, of Lancaster, S. C.
- 1834 Age 21. Attended his first series of lectures in medicine at Medical College of Charleston, S. C.
- 1835 Age 22. Was graduated from Jefferson Medical College, Philadelphia. Began practice of medicine in Lancaster, S. C., later moved to Mount Meigs, Alabama.
- 1836 Age 23. Married Theresa Jones, a niece of Dr. G. Churchill Jones, and had 7 children.
- 1840 Age 27. Moved to Montgomery, Alabama.
- 1845 Age 32. First began work on vesicovaginal fistula.
- 1851 Age 38. Taken ill with dysentery. Traveled north for health.
- 1852 Age 39. Described the position now known by his name and an operation for vesicovaginal fistula.
- 1853 Age 40. Moved to New York, Madison Ave. and 29th St.
- 1855 Age 42. Founder of a hospital for women at 83 Madison Ave. in New York City. In 1857 this became the Woman's Hospital of the State of New York.
- 1861 Age 48. For political reasons during Civil War moved to Europe where he lived in London and Paris for six years. Warmly received by leading physicians and surgeons, before whom he repeatedly performed his operation for vesicovaginal fistula.

- 1868 Age 55. Made Governor and Senior Consulting Surgeon of Woman's Hospital, New York.
- 1870 Age 57. Surgeon-in-Chief of Anglo-American Ambulance Corps in Franco-Prussian War.
- 1872 Age 59. Member of Board of Surgeons, Woman's Hospital.
- 1874 Age 61. Resigned from Woman's Hospital because outsiders were stopped from visiting his clinics and cancer patients were refused admission. Shortly before his death he became member of the consulting board.
- 1876 Age 63. President of American Medical Association.
- 1880 Age 67. President of American Gynecological Society.
- 1881 Age 68. Attended President Garfield after the attempted assassination.
- 1883 Age 70. Died Nov. 13, quietly and painlessly in bed. Buried in Greenwood Cemetery, New York City.

(1894) European and American admirers erected a statue to his memory in Bryant Park, New York City. In 1936 this statue was removed to Fifth Avenue at 103rd Street, opposite the New York Academy of Medicine.

Fellow of the Royal Academy of Medicine in Brussels.

Fellow of the Obstetrical Society of London.

Received the Order of the Knights of the Legion of Honor from France.

Received the Iron Cross from Germany.

Received the Order of Leopold I from Belgium.

Also decorated by the Governments of Italy, Spain, Portugal.

Honorary member of the Edinburgh, Brussels, Berlin, Christiania, Paris and Dublin medical societies.

Member of the Alabama State Medical Association.

Member of the New York State Medical Society.

Member of the New York Academy of Medicine.

Member of the New York Neurological, Pathological and Surgical societies.

Honorary member of the Connecticut, Virginia, South Carolina and California State medical societies.

EPONYMS

DEPRESSOR: A loop of stout wire used in depressing the anterior vaginal wall in examinations.

METHOD: Of treating trismus nascentium.

OPERATION: For vesicovaginal fistula.

POSITION: The semiprone position; patient on the left side and the chest, the right knee and thigh drawn up, the left arm along the back.

SPECULUM: A form of duck-billed vaginal speculum.

SUTURE: A shotted or clamp suture.

BIBLIOGRAPHY OF WRITINGS

1. Double congenital hare-lip—absence of the superior incisors, and their portion of alveolar process. *Amer. Jour. Dental Sc.*, 5: 51-56, 1844.
2. On the extraction of foreign bodies from the meatus auditorius externus. *Amer. Jour. Med. Sc.*, 9: 336-342, 1845.
2. Trismus nascentium, its pathology and treatment. *Ibid.*, 11: 363-379, 1846. Also: Philadelphia, Lea and Blanchard, 1864. 8°, 21 pp.
4. Removal of the superior maxilla for a tumor of the antrum. Apparent cure. Return of the disease. Second operation. Sequel. *Amer. Jour. Med. Sc.*, 13: 310-314, 1847.
5. Osteo-sarcoma of the lower jaw. Removal of the body of the bone without external mutilation. *Ibid.*, 14: 370-373, 1847.
6. Further observations on trismus nascentium, with cases illustrating its etiology and treatment. *Ibid.*, 16: 59-78; 354-366, 1848.
7. On the treatment of vesico-vaginal fistula. *Ibid.*, 23: 59-82, 1852. Also, rev.: *New York Med. Times*, p. 104, 1853. Also: New York, 1853. 8°, 28 pp. Also: Philadelphia, Lea and Blanchard, 1853. 8°, 28 pp.
8. Two cases of vesico-vaginal fistula, cured by J. Marion Sims of New York, late of Montgomery, Alabama. *New York Med. Gaz.*, 5: 1-7, 1854.
9. A case of vesico-vaginal fistula, with the os uteri closed up in the bladder; cured by J. Marion Sims of New York, late

- of Montgomery, Ala., with an illustration exhibiting the parts. *Amer. Med. Monthly*, 1: 109-112, 1854.
10. Report on Dr. Sim's lecture for a Woman's Hospital. *Ibid.*, 479-480, 1854.
 11. A case of vesico-vaginal fistula resisting the actual cautery for more than seven years; cured in thirteen days by the author's process. *New York Med. Times*, 3: 265-257, 1854. Also, abstr.: *Amer. Jour. Med. Sc.*, 28: 283 only, 1854.
 12. A new uterine elevator, with illustration. *Ibid.*, 35: 132-134, 1858.
 13. A review of silver sutures in surgery. An anniversary discourse before the New York Academy of Medicine, Nov. 18, 1857. New York, Wood, 1858. 8°, 79 pp. Also: New York, Wood, 1858. 20 pp. Also, rev: *North American Med. and Surg. Rev.*, 2: 635-653, 1858. Also: *New York Acad. Med. Anniversary Discourses*, Vol. 1.
 14. Amputation of the cervix uteri. *Tr. New York State Med. Soc.*, pp. 367-371, 1861. Also: New York, 1861. 8°, 16 pp.
 15. Vaginismus. *Amer. Med. Times*, 4: 310-311; 317-318, 1862. Also, abstr.: *Med. Times and Gaz.*, 2: 517 only, 1861. Also, abstr.: *Lancet*, 2: 477 only, 1861.
 16. On the method of uterine examination. *Ibid.*, 2: 413-416, 1864.
 17. Uterine polypi. *Ibid.*, 457-458; 542-544; 627-628, 1864. Speculum. *Ibid.*, 501-502, 1864.
 18. Influence of uterine displacements upon the sterile condition. *Med. Times and Gaz.*, 2: 208-209, 1865. Also, abstr.: *Amer. Jour. Med. Sc.*, 50: 557-558. 1865. Also, abstr.: *Brit. Med. Jour.*, 2: 190 only, 1865.
 19. Painful menstruation. *Lancet*, 1: 224-225; 253-254; 338-339; 587-588; 2: 42 only, 1865.
 20. Dilatation or division of the cervix uteri. *Ibid.*, 1: 440-441, 1865.
 21. Chronic inversion of the uterus. *Brit. Méd. Jour.*, 2: 541 only, 1865. Also, abstr.: *Med. Times and Gaz.*, 2: 537 only, 1865. Also, abstr.: *Lancet*, 2: 538 only, 1865.

22. *Procedentia uteri*. Abstr. *Lancet*, 2: 677-678, 1865. Also, abstr.: *Brit. Med. Jour.*, 2: 666-667, 1865. Also, abstr.: *Amer. Jour. Med. Sc.*, 51: 554-555, 1866.
23. *Clinical notes on uterine surgery; with special reference to the management of the sterile condition*. *Lancet*, 1: 17-20; 74-78; 114-115; 214-218; 263-265; 418-420, 1865. *Rev.*, *Ibid.*, 1: 125-126, 1866. Also: New York, Wood, 1866. 8°, 401 pp. Also: London, Hardwicke, 1866. 8°, viii, 436 pp. Also: *Klinik der Gebärmutterchirurgie mit besonderer Berücksichtigung der Behandlung der Sterilität*. Deutsch brsg. von Hermann Beigel. Erlangen. Enke, 1866. 8°, xiii, 333 pp. Also: *Notes cliniques sur la chirurgie utérine dans ses rapports avec le traitement de la stérilité*. Traduites de l'Anglais par le Dr. Lheritier. Paris, Masson, 1866. 8°, vi, 500 pp. Also: New York, Wood, 1867. 8°, xi, 401 pp. Also: New York, Wood, 1869. Also: In German. 2 Aufl., Erlangen, Enke, 1870, 8°, xi, 352 pp. Also: New York, Wood, 1871. 8°, xi, 401 pp. Also: New York, Wood, 1873. Also: In German, 3 Aufl., Erlangen, Enke, 1873. 8°, xii, 362 pp. Also: New York, Wood, 1886.
24. *Ovariectomy*. Pedicle secured by silver wire, after the failure of the actual cautery to arrest hemorrhage. *Brit. Med. Jour.*, 1: 50-51, 1867. Also, Abstr.: *Amer. Jour. Med. Sc.*, 53: 548-550, 1867.
25. On the nitrous oxide gas as an anesthetic. *Brit. Med. Jour.*, 1: 349-350, 1868.
26. Illustrations of the value of the microscope in the treatment of the sterile condition. *Ibid.*, 205 only; 465-466, 492-494, 1868.
27. *The Woman's Hospital Anniversary*. Address delivered at the Woman's Hospital, New York, Nov. 17, 1868. New York, Baker and Godwin, 1868. 11 pp.
28. On the microscope as an aid in the diagnosis and treatment of sterility. *New York Med. Jour.*, 8: 393-413, 1869. Also: New York, Appleton, 1869. 8°, 25 pp.
29. *Ovariectomy*. Pedicle secured by silver wire. Ligature. Cure. *Brit. Med. Jour.*, 1: 326 only, 1869.

30. Anglo-American ambulance. London, Harrison and Sons, 1870. 8°, 20 pp.
31. Kennedy's concentrated extract of *pinus canadensis*. Med. Gaz., 7: 69-70, 1871.
32. On ovariectomy. New York Med. Jour., 16: 561-617, 1872; 17: 360-387, 1873. Also: New York, Appleton, 1873. 8°, 85 pp. (Same) Ueber Ovariectomie. Deutsch von Hermann Beigel. Erlangen, F. Enke, 1873. 1 p. 1., 105 pp.
33. Nélaton's method of resuscitation from chloroform narcosis. Brit. Med. Jour., 2: 239-241, 1874. Also, abstr.: Amer. Jour. Med. Sc., 68: 570-573, 1874.
34. On intra-uterine fibroids, with illustrations of methods, etc. New York Med. Jour., 19: 337-360, 1874. Also: New York, Appleton, 1874. 8°, 27 pp. (Same) Tumores fibrosos intra-uterinos. Trad. al español por Agustin Danssa. Barcelona, N. Ramirez y Ca., 1875. 8°, 29 pp.
35. Utero-gastrotomy. Med. Rec., 10: 107-108, 1875. Also, abstr.: Amer. Jour. Med. Sc., 69: 582-583, 1875.
36. Lecture on vesico-vaginal fistula. Pac. Med. and Surg. Jour., 1875. Also: Med. Herald, Leavonworth, 1875.
37. Legislation and contagious diseases. Address as President of the American Medical Association, Jan. 6, 1876. Trans. Amer. Med. Ass., 27: 91-111, 1876. Also, ext.: Philadelphia, Collins, 1876. 8°, 14 pp. Also: London, Spottiswoode, 1876, 8°, 28 pp. Also, ext.: London, Spottiswoode, 1876, 8°, 16 pp.
38. Epithelioma of the cervix uteri. Abstr.: Brit. Med. Jour, 2: 277 only, 1876.
39. The Woman's Hospital in 1874. A reply to the printed circulars of Dr. E. R. Peaslee, T. A. Emmett, and T. Gailard Thomas's address to the medical profession, May 5, 1877. New York, Kent and Co., 1877. 8°, 24 pp.
40. The discovery of anesthesia. Richmond Med. Monthly, 4: 1877. Also: Richmond, J. W. Ferguson & Co., 1877. 20 pp. Also: Richmond, 1877; New York, 1879. 8°, 14 pp.

41. Professor Lister's Introduction on antiseptic surgery. *Brit. Med. Jour.*, 2: 608-609, 1877.
42. Battey's operation. *Ibid.*, 2: 793-794, 840-842, 881-882, 916-918, 1877. Also: London, 1878. 8°, 31 pp. Also, ext.: London, 1878, 8°, 2 pp.
43. Sterility in women. *Johnson's Cyclopaedia*, 1877.
44. Obituary. Gustav Simon. *Amer. Jour. Obst.*, 10: 80-83, 1877. Also: New York, 1877. 8°, 7 pp.
45. Cholecystotomy for the removal of gall-stones in dropsy of the gall-bladder. *Brit. Med. Jour.*, 1: 811-815, 1878. Also: London, 1878. 12°, 20 pp. Also: *Gaillard's Med. Jour.*, 1878. Also, in French: *Rev. de Lit. Méd. pour* 1878, 3: 564, 1878; 4: 34; 78; 107; 250; 278-280; 400-402; 1879. Also, in French: *J. de méd. chir. et pharmacol.*, *Brux.*, 68: 418-424; 499-510, 1879.
46. The operations of Simpson and Sims for stenosis of the cervix uteri compared. *Abst.: Brit. Med. Jour.*, 2: 365-366, 1878. Also: *Gaillard's Med. Jour.*, 1878.
47. Surgical instruments exhibited at International Exhibition in Paris: uterine curette, bistoury holder, uterine dilator. *Brit. Med. Jour.*, 2: 704-705, 1878.
48. On the extraction of foreign bodies from the ear. *Ibid.*, 282; 868-869, 1878.
49. On the surgical treatment of stenosis of the cervix uteri. *Tr. Amer. Gyn. Soc.* 1878, 3: 54-100, 1879.
50. History of the discovery of anesthesia. *Virginia Med. Monthly*, 1879. Also: *Gaillard's Med. Jour.*, 1879. Also: New York, 1879. 8°, 14 pp.
51. On syringing the ear. Letter. *Brit. Med. Jour.*, 1: 140 only, 1879.
52. A forceps case. Letter. *Ibid.*, 1: 282 only, 1879.
53. Diagnosis of abscesses of the liver by symptoms of cerebral hyperaemia, with some remarks on the treatment of hepatic abscess by aspiration. *Trans. Virginia Med. Soc.*, 3: 106-111, 1879. Also; *Southern Practitioner*, 2: 97-103, 1880. Also: Richmond, 1879. 8°, 6 pp.
54. The treatment of epithelioma of the cervix uteri. *Amer.*

- Jour. Obst., 12: 451-489, 1879. Also: Gaillard's Med. Jour., 29: 625-643, 1880. Also: New York, Wood, 1879. 8°, 41 pp. Also, in French: Ann. de gynec., Par., 13: 401-422, 1880.
55. The bromide of ethyl as an anesthetic. New York Med. Rec., 17: 361-365, 1880. Also, abstr.: Brit. Med. Jour., 1: 746 only, 1880. Also: Gaillard's Med. Jour., 29: 530-546, 1880. Also: New York, 1880. 8°, 22 pp.
56. Thomas Keith and ovariectomy. Surgeons in public journals. Amer. Jour. Obst., 13: 290-303, 1880. Also: Med. Rev., New York, 17: 103, 1880. Also: New York, Wood, 1880. 8°, 16 pp.
57. Pregnancy vomiting. Arch. Med., 3: 269-276, 1880. Also: New York, Putnam, 1880. 8°, 8 pp. Also: Gaillard's Med. Jour. 1880.
58. Annual address as President of the American Gynecological Society. Trans. Amer. Gyn. Soc., 5: 25-37, 1881. Also: Gaillard's Med. Jour., 5, 1881.
59. Remarks in W. O. Baldwin's On the poisonous properties of quinine. Med. Gaz., Oct. 22, 1881.
60. Remarks on the treatment of gunshot wounds of the abdomen in relation to modern peritoneal surgery. Brit. Med. Jour., 2: 925-926; 971-973, 1881; 1: 184-186; 222-223; 260-262; 302-304, 1882. Also: Gaillard's Med. Jour., 1882.
61. The surgical treatment of President Garfield. North American Rev., New York, 133: 594-601, 1881.
62. Treatment of syphilis. Brit. Med. Jour., 1: 448-450, 1883. Also: Indianapolis, 1883. 8°, 7 pp. (Same) 2. ed., Indianapolis, 1883. 8°, 7 pp.
63. The story of my life. Edited by his son, H. Marion Sims, M. D. New York, Appleton, 1884. 12°, 471 pp. Also: New York, Appleton, 1885. 8°, 471 pp. Also: New York, Appleton, 1888. 8°, 471 pp.

BIBLIOGRAPHY OF BIOGRAPHIES

- Ode to Dr. Marion Sims. By H. L. Med. Times and Gaz., 1: 216, 1866.
- Biography. Richmond and Louisville Med. Jour., 15: 92-95, 1873.
- Biography by H. L. Stuart. Virginia Med. Month., 3: 731-743, 1877.
- To the medical profession. Statements respecting the separation of Dr. J. Marion Sims from the Woman's Hospital, New York. By E. R. Peaslee, T. A. Emmett and T. G. Thomas. (Reply to Sim's pamphlet entitled "The Woman's Hospital in 1874.") New York, 1877.
- Editorial interview with Dr. J. Marion Sims; a full exposition of the points in the controversy between Drs. Peaslee, Emmet and Thomas and Dr. Sims. By W. Hazard. St. Louis Clin. Rec., 4: 153-172, 1877.
- Dr. Marion Sims and his operations in Vienna. By F. Barker. Med. Rec., 14: 376, 1878.
- Biography in Physicians and Surgeons in the United States. Edited by W. B. Atkinson. Philadelphia, Robson, 1878, pp. 48-49.
- Biography. Boston Med. and Surg. Jour., 109: 501, 1883.
- Biography. New York Med. Jour., 38: 550, 1883.
- Biography. Jour. Amer. Med. Ass., 1: 659, 1883.
- Biography. Med. News, 43: 555, 1883.
- Biography. Med.-Leg. Jour., 1: 471, 1883-4.
- Biography. Med. Rec., 24: 557, 1883.
- Biography. Virginia Med. Month., 10: 631-638, 1883-4.
- Biography. Gaillard's Med. Jour., 36: 601-604, 1883.
- Biography. Brit. Med. Jour., 2: 995, 1883.
- A memoir of J. Marion Sims. By T. A. Emmet. New York Med. Jour., 39: 1-5, 1884. Also: New York, Appleton, 1884. 8°, 19 pp.
- Biography by F. Howitz. Gynaek. og obst. Medd., Kjøbenh., 5: 1-3, 1884.
- Biography by P. F. Munde. Amer. Jour. Obst., 17: 52-61, 1884.

- Tribute to the late James Marion Sims. By W. O. Baldwin. Gaillard's Med. Jour., 37: 1-9, 1884. Also: Montgomery, Ala., 1884. 8°, 31 pp.
- Biography by W. M. Carpenter. Tr. Med. Soc. New York, pp. 400-405, 1884.
- In memoriam. Eulogy pronounced at the funeral of J. Marion Sims, November 16, 1883. By Rev. Charles Parkhurst. New York, Putnam, 1884. 12°, 16 pp.
- The story of my life. Edited by his son, H. Marion Sims, M.D. New York, Appleton, 1884. 12°, 471 pp. Also: New York, Appleton, 1885. 8°, 471 pp. Also: New York, Appleton, 1888. 8°, 471 pp.
- Biography by J. M. Toner. Gaillard's Med. Jour., 32: 127-134, 1884.
- Biography by W. G. Wylie. New York Med. Jour., 39: 405; 432, 1884. Also: New York, 1884. 8°, 26 pp.
- Biography. New England Med. Month., 4: 204-207, 1884.
- Biography by E. Vande Warker. Tr. Amer. Gynec. Soc., 1884, 9: 398-403, 1885.
- Biography by J. S. B. Tr. Amer. Surg. Ass., 1884, 2: xxxviii, 1885.
- In memoriam. By W. M. Carpenter. New York, Stettiner, Lambert and Co., 1886. 8°, 18 pp.
- Biography. Med. Mirror, 1: 469-471, 1890.
- Reminiscences of J. Marion Sims; incidents of his early professional life; discovery of his speculum; peculiarities. By T. A. Means. Alabama Med. and Surg. Age, 6: 607-616, 1893-4.
- J. Marion Sims, the father of modern gynecology. By P. F. Munde. Med. Rec., 46: 514, 1894.
- J. Marion Sims, surgeon and philanthropist. By G. F. Shrady. Ibid., 513, 1894.
- The Sims memorial statue. Amer. Jour. Obst., 30: 712-720, 1894.
- Reminiscences of J. Marion Sims in Paris. By E. Souchon. Med. Rec., 46: 705-708, 1894. Also: Texas M. J., 10:

399-405, 1894-5. Also: Tr. South. Surg. & Gynec. Ass., 1894, 7: 27-38, 1895.

Places rendered famous by Marion Sims, in Montgomery, Ala.; notes on a trip to the meeting of the American Surgical Association in New York, May 1895. By E. Souchon. New Orleans Med. and Surg. Jour., 23: 455-460, 1895-6. Also: New Orleans, 1896. 8°, 18 pp.

J. Marion Sims and his work. By J. A. Wyeth. Med. Rec., 48: 694-700, 1895. Also: Tr. South. Surg. & Gynec. Ass., 1895, 8: 9-39, 1896.

Ueber Marion Sims und seine Verdienste um die Chirurgie. By R. Olshausen. Berlin, 1897. 8°, 30 pp.

Biography. Practitioner, Lond., 60: 61-54, 1898.

The life and work of J. Marion Sims. By W. D. Ward. Amer. Jour. Obst., 54: 192-203, 1906.

Biography. A historic parallel. By G. M. Gould. Biog. Clinics, 5: 383-388, 1907.

Biography by J. H. Allen. J. South Carolina Med. Ass., 7: 43-47, 1911.

Biography by W. L. Lowder. Charlotte, N. C., Med. Jour., 66: 93-101, 1912.

Biography by C. Cleveland. Amer. Jour. Obst., 67: 954-955, 1913.

Biography by A. Martin. Monatschr. f. Geburtsch. u. Gynaek., 37: 217, 1913. Also: Zeitschr. f. Geburtsch. u. Gynaek., 73: 946-948, 1913.

Biography by A. Allemann. München. med. Woch., 60: 138, 1913.

Biography. Album Amer. Gynec. Soc., p. 442, 1918.

Ephraim McDowell and J. Marion Sims, the American founders of gynecology. United States Nav. Med. Bull., 14: 373, 1920.

Sketch of life. By J. M. King. Jour. Tennessee Med. Ass., 13: 365-368, 1921.

Biography by H. A. Royster. Surg., Gynec. and Obst., 35: 237-239, 1922.

- Biographical sketch by O. Clark. *Brazil-medico*, 36: 308, 1922.
- Biography by H. C. Semple. *Amer. Med.*, Burlington, Vt., n.s. 18: 639-646, 1923.
- Biography. *Virginia Med. Monthly*, 50: 494, 1923.
- Biography. *Med. Jour. and Rec.*, 122: 687-689, 1925.
- Biography. *Clin. Med.*, Chicago, 33: 535-536, 1926.
- Biography by S. Brunson. *Jour. South Carolina Med. Ass.*, 22: 174-175, 1926.
- The Sims memorial address on gynecology. By D. Bissell. *Amer. Jour. Surg.*, 5: 526-534, 1928. Also, abstr.: *Jour. South Carolina Med. Ass.*, 24: 9-11, 1928.
- Landmarks in surgical progress: J. Marion Sims and vesico-vaginal fistula. By I. S. Cutter. *Internat. Obst. Surg.*, 47: 173-175, 1928.
- Biographical sketch in *Dictionary of American Medical Biography*. New York, Appleton, 1928.
- Genito-urinary fistula in female, with appreciation of Sims and his work. By D. Bissell. *Proc. Roy. Soc. Med. (Sect. Obst. and Gynec.)*, 22: 1-18, 1928. Also: *Amer. Jour. Surg.*, 7: 143-156, 1929.
- J. Marion Sims, surgeon and humanitarian. By D. Bissell. *Amer. Jour. Surg.*, 6: 561-565, 1929.
- Biography by S. Leigh. *Virginia Med. Monthly*, 56: 502-506, 1929.
- Sims memorial unveiled May 10, 1929, in Columbia, S. C. Columbia, 1929. 20 cm., 29 pp.
- Eponyms: James Marion Sims. *Amer. Jour. Surg.*, 8, suppl.: 498-499, 1930. Also in: *Abdominal cavity and peritoneum*. By E. M. Livingston. New York, Hoeber Co., 1930. pp. 82-83.
- Biography by C. K. Weil. *South. Med. Jour.*, 23: 670-671, 1930.
- Biographical brevities: Sims' position. *Amer. Jour. Surg.*, 13: 578, 1931.
- An appreciation. By I. Abell. *South. Med. Jour.*, 26: 1013-1019, 1933.
- J. Marion Sims, father of gynaecological surgery. By Jennie MacMaster. *The trained Nurse and Hosp. Rev.*, 92: 121-127, 1934.

Sims' statue. New York Times, Feb. 23, 1934. Also: New York Times, Oct. 21, 1934.

Address at the rededication of the Sims' memorial, Oct. 20, 1934. By J. H. Finley. New York, 1934. 2 l., 24 cm.

Sims and origin of modern gynecology. By G. G. Ward. Bull. New York Acad. Med., 12: 93-104, 1936.

Sims, father of modern gynecology. By S. Harris. South. Surgeon, 6: 35-52, 1937.

The "Scotch-Irish" of the valley of Virginia, and their influence on medical progress in America. By H. H. Trout. Ann. Med. Hist., 10: 71-82, 1938.

INTRODUCTION

Like McDowell, Sims was born in rural America, but not until 1813, forty-two years after McDowell's birth. He received the best medical education obtainable, graduating from Jefferson Medical College in 1835. He then began practice in Alabama and rapidly became known as a capable and original surgeon. Surgery had advanced since the days of McDowell. In 1835 Sims operated successfully for an abscess of the liver and two years later he removed both the upper and lower jaw of a patient. But when Sims began to practice Lister's earliest work on anti-sepsis was thirty-two years in the future and anesthesia was unknown. Sims' surgery was far from that which we know today.

In 1845 Sims was called to attend a woman who had fallen from a horse. His examination disclosed a displacement of the uterus. In making a digital examination by the vaginal route with the patient on her knees, Sims was suddenly unable to feel the displaced uterus and the patient was relieved of her complaint. As the patient was turned onto her back Sims noticed a sudden expulsion of air from the vagina. He immediately guessed that the patient's knee-chest position aided the replacement of the uterus. He determined to use this position as a routine for vaginal examination. To aid him he devised a special speculum which allowed air to enter the vagina so that its walls could be more readily visualized. Later Sims found that the left lateral posture was equally as effective for vaginal examination as the knee-chest position.

Sims then became interested in a very troublesome condition which had resisted operative treatment; namely, vesico-vaginal fistula. Sims was able to repair the fistula successfully because of four principles; namely, 1. The left lateral posture made visualization easier and better; 2. The vaginal speculum exposed the fistula opening; 3. A special silver wire suture effectively held the repaired tissues until healing could take place; and 4. The bladder was kept empty by a catheter until the fistulous tract had healed. Sims' first report *On the treatment of vesico-vaginal fistula* of 1852 is reproduced completely in the following pages.

Sims removed to New York in 1853 where he was instrumental in establishing the State Hospital for Women two years later. He visited Europe in 1861 and performed his fistula operation before most of the leading surgeons of the time. He originated several operations on abdominal organs and was one of the greatest surgeons of his day. His work forms an excellent adjunct to that of McDowell's. Together these two men paved the way for modern surgery within the abdomen.



On the Treatment of Vesico-Vaginal Fistula

BY

J. MARION SIMS, M.D.

Montgomery, Ala.

[With twenty-two wood-cuts]

Published in *The American Journal of the Medical Sciences*, Philadelphia, 1852, New Series, Vol. XXIII

VESICO-VAGINAL FISTULA—an abnormal communication between the bladder and vagina, allowing an involuntary discharge of urine—is produced generally by tedious labour. The impacted foetal head, jamming the anterior vaginal parietes against the symphysis pubis, obstructs the circulation of the parts, which results in a slough of greater or less extent, according to the degree and duration of the impaction. Almost the only hope of preventing so serious a disaster under such circumstances is the timely resort to instrumental delivery. By this means I have seen the slough confined to the vaginal mucous membrane, where, otherwise, it would unquestionably have extended entirely through the vaginovesical septum. It occurs principally in first labours where the pelvis is small, the soft parts unyielding, and the foetal cranium large; but I have seen it in those advanced in life, who had given birth previously to many children. Authors are disposed to attribute the accident, in many cases, to the awkward use of obstetrical instruments; but, from a careful analysis of these

cases, and from my own experience, I am well satisfied that for one case thus produced, their judicious application has prevented it fifty times.

Other causes produce it occasionally, such as a prolonged retention of a pessary in the vagina, a calculus or other foreign body in the bladder, abscesses, venereal ulcerations, &c. I have seen one case where the whole base of the bladder was destroyed by a corroding ulcer, which, originating in the cervix uteri, extended forward to the urethra. Whatever may be the cause of this distressing affection, it is a matter of serious importance to both surgeon and patient that it be rendered susceptible of cure.

Its diagnosis is sufficiently easy. Incontinence of urine, following a tedious labour after a lapse of from one to fifteen days, will always prove its existence. But to determine the exact size, shape, and relative position of the artificial opening requires some nicety of examination. The consequences of the involuntary discharge of urine are indeed painful. The vagina may become inflamed, ulcerated, encrusted with urinary calculi, and even contracted; while the vulva, nates, and thighs are more or less excoriated, being often covered with pustules having a great resemblance to those produced by tartar emetic. These pustules sometimes degenerate into sloughs, causing loss of substance, and requiring a long time to heal. The clothes and bedding of the unfortunate patient are constantly saturated with the discharge, thus exhaling a disagreeable effluvium, alike disgusting to herself and repulsive to others.

The accident, *per se*, is never fatal; but it may well be imagined that a lady of keen sensibilities so afflicted, and excluded from all social enjoyment, would prefer death. A case of this kind came under my observation a few years (p. 60) since, where the lady absolutely pined away and died, in consequence of her extreme mortification on ascertaining that she was hopelessly incurable.

The relative position of the fistula has served generally as the basis of a classification. Thus we have:—

- 1st. The urethro-vaginal, where the fistula is confined to the urethra.

2d. Those fistulæ situated at the neck of the bladder, or root of the urethra, destroying the *trigonum vesicalis*.

3d. Those of the body and *bas-fond* of the bladder, of which, Velpeau says, "there is no fact, up to the present time, which proves indisputably that they have ever been cured."

4th. The utero-vesical, where the opening communicates with the body or cervix of the uterus.

I have never met with one of the last-named class; but of the others I have seen a great variety, embracing almost every possible shape and size.

The position of the patient for the operation, the speculum, the means of vivifying the edges of the fistulous opening, the suture apparatus, and the catheter which I shall describe, are, I believe, original with myself, having been suggested by the peculiarities of individual cases. The final perfection of these mechanical contrivances has been the slow work of experiment.

At the first, I had three cases, upon which I operated about forty times, but failed in every instance to effect a perfect cure, though succeeding so far as to encourage me to persevere. Now, I think I may say that almost every case of this hitherto intractable affection is rendered perfectly curable.

Before detailing my operation, it may be interesting historically to take a brief survey of the surgery of this disease up to the present time.

For the last half century, though surgeons have laboured assiduously to cure it, they have almost always been unsuccessful. Cases have, now and then, been remedied, but they were so few that no general principles of treatment could be established, and, consequently, no certainty of success, in any single instance, could be predicated.

The *suture* was, of course, the first surgical appliance that suggested itself to the mind of operators. It was used in all its various modifications without success. The great difficulty of applying the suture, and its signal failure, caused surgeons to invent a number of instrumental apparatuses, all of which are clumsy and complicated.

As a curiosity, let me here introduce a description of the ap-

paratus of Lallemand, the distinguished professor, of Montpellier:—

"It is composed—1st, of a large canula about four inches long; 2d, of a double hook, which is moved in the principal instrument by means of a stem, in such manner as to push it out, or to make it enter its sheath; 3d, of a circular plate which terminates the other extremity of the canula, and which would hinder, if necessary, this latter from penetrating too deep into the urethra; and, 4th, of a cork-screw spring, intended to draw forward the small hooks as soon as they are inserted in the posterior lip of the fistula. The canula, being passed into the bladder, allows of our pushing the two small hooks into the vagina through the vesico-vaginal septum, which latter is supported by the left (p. 61) fore-finger. By making a turn of the screw, they are kept in this position; a pledget of lint, or fine linen, designed for protecting the tissues, is then placed between the front part of the urethra and the external plate of the canula; finally, we relax the spring which acts then, at the same time, by making traction on the posterior lip with its hooks, and by pressing backwards the lower wall of the urethra by means of the circular plate, or the lint, which serves as its *point d'appui*. By a mechanism which would be too long for description, we may regulate the stop of the spring in such manner that there will only result from it a moderate degree of pressure, though sufficient for bringing the two borders of the fistula in contact."—*Velpeau*, vol. iii. p. 852.)

The apparatuses of Lewziski, of Dupuytren, of Laugier, of Fabbri, and others, are equally complicated, quite as unfit to fulfill the proper indications of treatment, and, by experience, have proved as wholly worthless.

Others have attempted to improve different stages of the operation. Thus Colombat praises his spiroidal needle for passing a whip suture in longitudinal fistulas, and M. Sanson has proposed to enlarge the urethra by a double lithotome for the purpose of carrying the finger through the urethra into the bladder, merely to depress the fistula toward the vulval opening; while Wutzer proposes, and performs in a great number of cases, the high operation of paracentesis vesicæ, confining his patient for several days on her abdomen, by means of cushions, straps, and buckles.

These are referred to as historical facts, and not for any good that could possibly result from them.

While all these formidable contrivances, and the suture, have failed so signally, *cauterization* has but little more to boast of in the way of success. Very small fistulous openings have occasionally been reported as cured by the application of the nitrate of silver, a catheter being retained in the bladder; but, in fistulas of any size, it has proved entirely abortive.

To show how utterly hopeless have been all our efforts heretofore, we may allude to the suggestion of some of the French surgeons to apply the Taliacotian method of anaplasty to this operation, which has actually been repeatedly performed by Roux, Jobert, and others; and, also, to the operation of M. Vidal, for an "obturation of the vulva," whereby the bladder and vagina become a grant compound receptacle of the urine and menstrual secretion. It is an idle waste of time to dwell longer on means so perfectly ineffectual, not to say mischievous.

But have no useful, practical suggestions been made, as yet, by any one on the treatment of vesico-vaginal fistula? Yes: two names stand out in bold relief amongst those who have devoted some time and attention to this subject. I allude to our own countryman, Mettauer, who uses leaden sutures; and to the indefatigable Jobert, who is the author of the operation of *autoplastie par glissement*. The first, by his plan, has cured several cases; while the latter has achieved a greater degree of success than any other surgeon.

Thus, all that we know on the subject worth knowing is due to America and France; while German and British surgery have done comparatively nothing for the amelioration of this loathsome and troublesome disease.

(p. 62) Many of our systematic works pass it over in silence, or dismiss it with a few remarks discouraging all attempts at treatment. Samuel Cooper, in his great *Surgical Dictionary*, does not introduce the subject even by name; while Liston devotes less than a page to it. Alluding to the application of the heated wire, he says: "By this means a small opening may occasionally be made to heal up. But when the communication is to a large extent, but little hope remains to the patient." Fergusson, Gibson, and others say nothing about it; while Millar dismisses

it as summarily as did Liston. But how could it be otherwise, when its mechanical treatment is so imperfect that no general principles could be laid down?

It is not my intention to allude to all that has been attempted by different surgeons; but it is equally a duty and a pleasure here to chronicle what has been done by our own countrymen who lay any claims to originality or credit.

The first successful case in this country is, I believe, by Dr. Hayward, of Boston. The following is his description of the operation:—

“The patient was placed on the edge of a table, in the same position as in the operation for lithotomy. The parts being well dilated, I introduced a large bougie into the urethra, and carried it back as far as the fistula. In this way I was able to bring the fistula downwards, so that the opening was brought fairly into view. The bougie being then taken by an assistant, I made a rapid incision with a scalpel around the fistula, about a line from its edges, and then removed the whole circumference of the orifice. As soon as the bleeding, which was slight, had ceased, I dissected up the membrane of the vagina from the bladder, all around the opening, to the extent of about three lines. This was done partly with the view of increasing the chance of union, by presenting a larger surface, and partly to prevent the necessity of carrying the needles through the bladder. I then introduced a needle, about the third of an inch from the edge of the wound, through the membrane of the vagina, and the cellular membrane beneath, and brought it out at the opposite side, at about an equal distance. Before the needle was drawn through, a second and a third were introduced in the same way; and these being found sufficient to close the orifice, they were carried through, and the threads tightly tied. Each thread was left about three inches in length.”—(*Am. Journ. Med. Sciences*, Aug. 1839.)

Besides this case, Dr. Hayward has recently reported eight others, operated upon since August, 1840, two of which were entirely successful. He says:

“The operation was done in every instance by ligature. The result has, on the whole, been satisfactory. Any thing that is calculated to remove this infirmity, or to lessen in the slightest degree the sufferings of the individuals who are afflicted with it, should be made known.

"I had never seen the operation done until I did it myself, nor could I find any description of the mode which others had adopted, that was sufficiently clear and explicit to be of much service. I had, therefore, to take such a course as I thought save, and at the same time likely to effect the object, viz: the closure of the fissure. I do not know that others may not have operated precisely in the same way; but if they have, I am not aware of it.

"I performed the operation twenty times, but it was done on nine patients only, one being operated on six times, another five, two twice, and five once."—(*Boston Med. and Surg. Journal*, vol. xliv., No. 11. April 16, 1851.)

Dr. Pancoast, of Philadelphia, has operated successfully in two cases, by the following method:—

"The peculiarity of the operation consists, virtually, in attaching the two sides of the abnormal opening firmly together, on the principle of the tongue and (p. 63) groove, so as to get four raw surfaces in contact, and thus increase the probabilities of union by the first intention. For this purpose it is necessary that the margins of the fistula should have considerable thickness, and when not found in this state, they are to be thickened by repeated applications of lunar caustic; or, better still, of the actual cautery.

Having exposed the fistulous orifice as thoroughly as possible with a Charrière's speculum, from which the sliding blade has been removed, an assistant at the same time drawing the vestibulum well up towards the front of the pubis, my first object in the operation is to split the most posterior margin of the fistula to the depth of half an inch. I next pare off the edges of the other lip of the fistula, so as to bring it into a wedge shape; first reverting it as much as possible with a small blunt hook, and trimming off the mucous membrane on the side next the bladder with the curved scissors or scalpel, and then detaching, in like manner, the vaginal mucous membrane, to the breadth of three-quarters of an inch, along the whole extent of the lip. This was a very difficult but most important part of the process. Having checked the bleeding by the use of astringent applications, my next object is to insert the raw wedge or tongue, into which one of the lips of the fistula has been converted, into the groove which has been cut in the other, and hold them in close connection. This I accomplish by the means of a peculiar suture that might be called the plastic, and in the same way that I have

described its application in reference to some plastic operations in my *Operative Surgery*; and in the *American Journal of the Medical Sciences* for October, 1842.

"When the sutures are knotted firmly, the tongue or wedge will be found immovably imbedded in the groove. The sutures I leave for two weeks or more, or until they become loose. A gum catheter should be kept in the bladder to prevent the accumulation of urine. To keep the inflammation from running to a destructive height, a bladder of cold water should be applied for thirty-six hours to the vulva.

"On the second or third day, I direct the frequent injection of a solution of zinci sulph. into the vagina, in order to increase the tone of the parts. On the fourth or fifth day, I apply to the line of union a solution of lunar caustic with a camel's hair pencil. This application should be made twice in the twenty-four hours, the solution being gradually increased in strength. Union by first intention may be expected to take place under this treatment to a considerable extent; at such points as it should fail to occur, union by second intention is to be promoted by the use of lunar caustic in substance, so as to raise a bed of granulations on the raw surfaces of the lips, while they are held in contact by the plastic suture.

"In one case, there was a complete destruction of a cross section of the whole urethral structure, near the neck of the bladder; in the other, there was an elongated orifice in the *bas-fond* of the bladder, which would more than admit the end of the finger."—(*Med. Examiner*, May, 1847.)

Dr. Mettauer's operation, the peculiarity of which consists in the use of leaden sutures, is described in the *Am. Journ. Med. Sciences* for July, 1847, to which I beg leave to refer the reader for particulars.

Having thus briefly alluded to what has been done, up to the present time, for the treatment of this affection, I shall now proceed to detail my own operation.

I conceive that I may claim originality: 1st. For the discovery of a method by which the vagina can be thoroughly explored, and the operation easily performed.

2d. For the introduction of a new suture apparatus, which lies imbedded in the tissues for an indefinite period without danger of cutting its way out, as do silk ligatures.

And 3d. For the invention of a self-retaining catheter, which can be worn (p. 64) with greatest comfort by the patient during the whole process of treatment.

Of the position of the patient for the operation.—With the exception of Velpeau and Chelius, all other operators, even Jobert, recommended that the patient be placed on the back as in the operation for stone.

Velpeau* says, "A round-shaped mattress is placed under the *belly*, in such manner as to enable her to keep her thighs flexed, *while lying upon her abdomen*. An assistant keeps the vagina dilated by means of a large gutter of metal, horn, or thin wood."

Chelius† directs "the patient to be placed on her *belly* upon a table covered with a mattress, so that she may kneel near its edge, with her head and chest bent forwards, and supported with small bolsters. The operator sits between the patient's thighs, upon a seat of proper height, so that his arms should not soon tire."

In 1845, previously to the translation of either Velpeau or Chelius, I hit upon the proper plan of exploring the vagina in these cases; but to the latter is due to the first published account of even a hint towards that method.

In order to obtain a correct view of the vaginal canal, I place the patient upon a table about $2\frac{1}{2}$ by 4 feet, on her knees, with the nates elevated, and the head and shoulders depressed. The knees must be separated some 6 or 8 inches, the thighs at about right-angles with the table, and the clothing all thoroughly loosened, so that there shall be no compression of the abdominal parietes. An assistant on each side lays a hand in the fold between the glutei muscles and the thigh, the ends of the fingers extending quite to the labia majora; then, by simultaneously pulling the nates upwards and outwards, the os externum opens, the pelvic and abdominal viscera all gravitate towards the epigastric region, the atmosphere enters the vagina, and there, pressing with a weight of 14 lbs. upon the square inch, soon stretches this canal out to its utmost limits, affording an easy

* Operative Surgery, Am. edition, vol. iii. page 851.

† Chelius' Surgery, by South, Am. edition, vol. ii, page 191.

view of the os tincae, fistula, &c. To facilitate the exhibition of the parts, the assistant on the right side of the patient introduces into the vagina the lever speculum represented in Fig. 1, and then, by lifting the perineum, stretching the sphincter, and raising up the recto-vaginal septum, it is as easy to view the whole vaginal canal as it is to examine the fauces by turning a mouth widely open, up to a strong light. (See Fig. 4.) This method of exhibiting the parts is not only useful in these cases, but in all affections of the os and cervix uteri requiring ocular inspection. The most painful organic diseases, such as corroding ulcer, carcinoma, &c., may be thus exposed without inflicting the least pain, while any local treatment may be instituted without danger of injuring the healthy structures. By this method, also a proper estimate, anatomically, can be had of the shape and capacity of the vagina; for where there is no organic change, no contraction, and no rigidity of it from sloughs, ulcers, and cicatrices, and where the uterus is movable, this canal immediately swells out to an enormous extent, thus showing its great expansibility.

(p. 65) Fig. 1 represents the speculum. When introduced and held properly, it causes no pain whatever. It is well enough to have two or three of different sizes, so as to be prepared for any case. The one ordinarily used by me is about $2\frac{1}{2}$ inches from *a*, where it supports the sphincter, to its terminal extremity at *b*. Its concavity *c*, *c* serves to reflect a strong light down on the vagino-vesical septum, the seat of fistula. Its breadth from *d* to *e* is about $\frac{7}{8}$ ths of an inch, widening a little as it approaches the end, making it somewhat in the shape of a duck's bill. The handle is made strong and unyielding, because a considerable degree of leverage has to be exercised by it. The curve at *f*, being cushioned to prevent its hurting the forefinger, fits accurately over it. The whole instrument is made of German silver, the concavity being highly polished for reflecting the light.

A small, slightly convex spatula, Fig. 2 (of German silver), may occasionally be needed to press the urethra downwards against the symphysis pubis, when there is a very minute fistula in the neighbourhood of the trigonus vesicalis; (p. 66) particu-

larly if the urethral folds are very redundant. This will seldom be used, but is sometimes indispensable, not only in exploration, but in holding the healthy parts out of the way in passing sutures.

These simple instruments, with this position and a good light, are all that are necessary for obtaining an accurate view of the parts. If the vagina and outlet are ordinarily capacious, a good

Fig. 1.

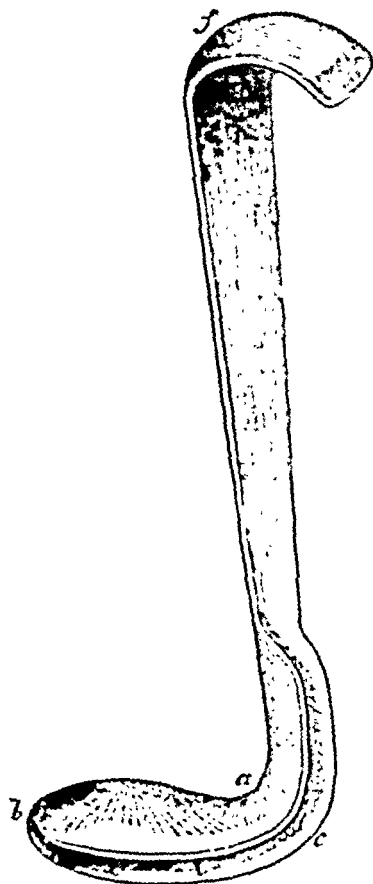
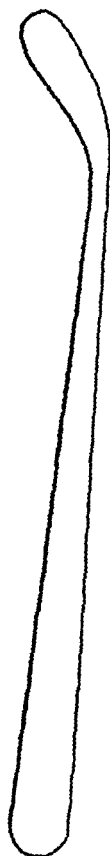


Fig. 2.



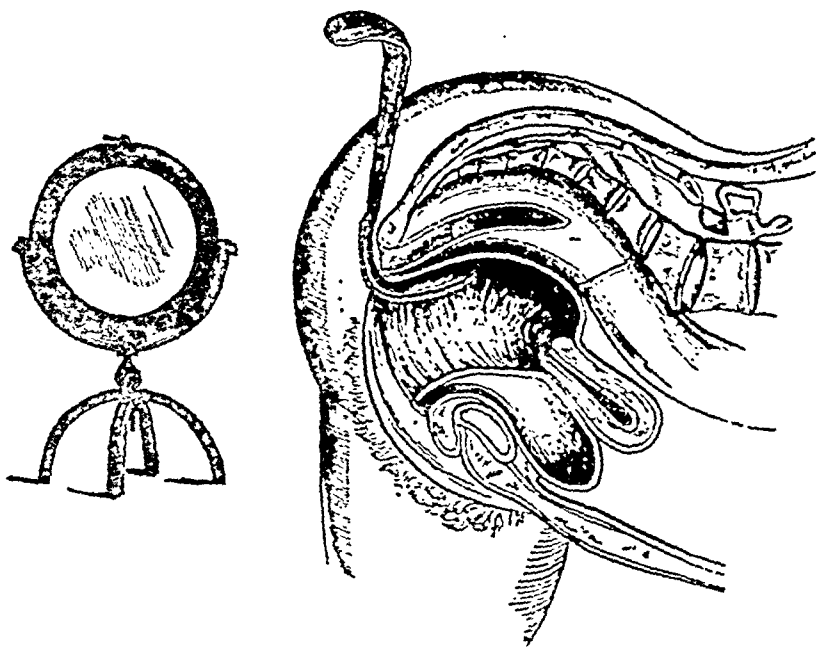
strong northern light, of a clear day, from a large solitary window, is all-sufficient. But if this canal has been narrowed by cicatrices after extensive sloughs, or from other causes, then sunlight is absolutely necessary for every stage of the operation from first to last. For this purpose, a small table is placed near a window admitting the sun-light. An assistant, sitting by, adjusts on the

table a glass, Fig. 3, some eight or ten inches in diameter, so as to throw the rays of light into the vagina, which, passing to the right of the operator, and striking the concave surface of the bright speculum, are reflected down on the anterior vaginal paries, making everything perfectly distinct.

Fig. 4 shows the speculum introduced, elevating and supporting the sphincter; also the relative position of the organs, when the patient is examined as directed; the vaginal canal being distended to its greatest capacity.

Fig. 3.

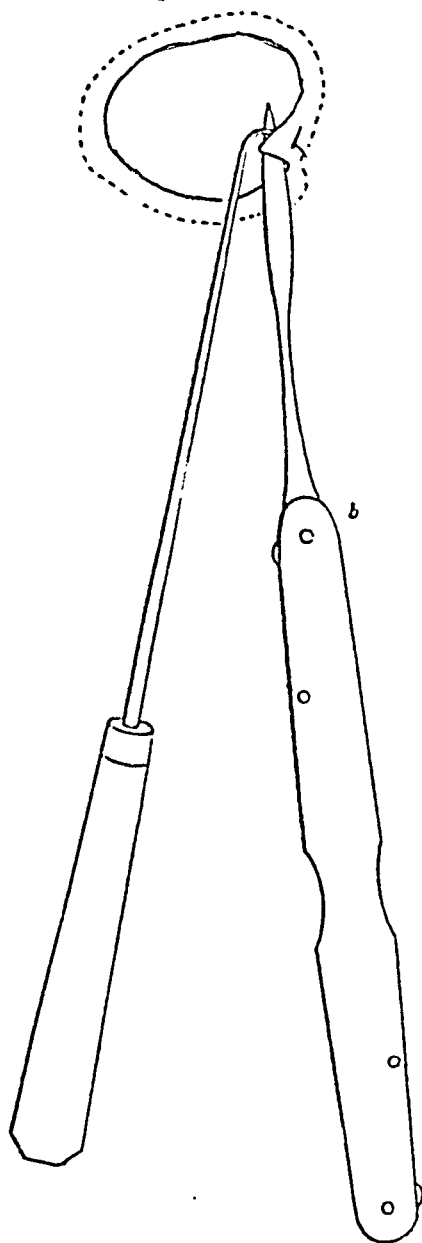
Fig. 4.



Of scarifying the edges of the fistulous opening.—This was the most tedious and difficult part of the operation with me, as it has always been with others. For three or four years, I had great trouble in getting such instruments (p. 67) made as I thought indicated; but those I now use for this purpose are so simple, that they can be had anywhere. A delicate tenaculum, Fig. 5, *a*, and a sharp-pointed knife, Fig. 5, *b*, are alone necessary.

The tenaculum, Fig. 5, *a*, is very small; the curve being at right angles with the shaft, and not more than one-third of an

Fig. 5.



inch long. If longer, it is not easily managed, nor so generally applicable to any and every part of the fistula. The shaft, some five or six inches long, it set into a firm handle. Of this

size and shape, it can be used to elevate the edge of the opening with equal facility, whether laterally or otherwise; while, if curved at more than a right angle, it can be useful only in hooking up and drawing forward the anterior and posterior margins.

Fig. 5 represents the tenaculum *a*, hooking up and elevating the edge of a fistula, while the point of the knife *b* is applied, ready to separate the part so raised up. This process is continued till the edge of the opening is well vivified all round (as seen by the dotted line), sometimes removing a strip an inch or more long before it is cut or torn off. The denudation is to be from a quarter to the third of an inch wide. I have often made the mistake of not removing enough of the callous edge; but I now take good care to remove it freely, extending the scarification up on the vaginal surface. I do not remove any of the lining membrane of the bladder, unless it is very much altered in character, and projects through the fistula into the vagina in such a way as to obstruct the easy performance (p. 68) of the operation; which rarely happens, and only where there is a great loss of substance.

Where the fistula is very small, say not larger than a common-sized probe, or even as small as a number seven or eight sewing needle, the best plan to scarify is, to hook up the part with the tenaculum, pull it forward, and by a thrust of the knife transfix the entire thickness of the vagino-vesical septum; then by a circular sweep of the instrument, the whole fistulous track may be removed at once; which substitutes for the small and callous opening, a smoothly cut orifice of rather a conical shape, large enough to admit the end of the forefinger.

Where the fistula is so small, there is always an abundance of tissue, and there need be no fear of removing the parts freely; for it is easier to close properly an opening as large as the end of the finger, than a smaller one, provided there is no scarcity of texture.

Where the fistula, on the other hand, is very large, there is occasionally some trouble in determining exactly what to cut; because by the bearing down, sobbing, straining, or even voluntary resistance of the patient, the mucous membrane of the bladder may be forced out in voluminous folds, so as to render

the fistulous edges indistinct, and there is danger of scarifying, either too high up on the vaginal surface, or too far in on the vesical lining. To obviate this difficulty, a properly curved metallic bougie may be passed through the urethra up to the fundus of the bladder; thus putting the parts on the stretch and carrying back into its cavity, the apparently redundant lining. The bougie curved down between the thighs may be held by a third assistant. But I greatly prefer to introduce a bit of soft sponge, of proper size, into the cavity of the bladder, which forces back the lining membrane, leaving the fistulous boundary distinct, when the scarification may be easily accomplished. The introduction of the sponge into the cavity of the bladder, or merely between the edges of the fistula, as well as its removal, is always attended with very great pain. Once introduced, I allow it to remain, till the sutures are passed and ready to be secured.

During the scarification, there is, of course, always hemorrhage; and, in some instances, it is so profuse as to compel us to desist for a short time, the patient being allowed to change her position and rest. As soon as the bleeding ceases, the operation may be resumed.

To remove the blood from the cut surface during the scarification, a probang is necessary (Fig. 6), which is made by tying a nice bit of sponge to the end of a piece of whalebone some eight or ten inches long. It is well enough to have two or three of these, which will keep one assistant pretty busy to wash clear of blood at this stage of the process. The probang can generally (p.69) be best applied by the operator, as his position allows him to see exactly where it is most needed.

I cannot lay too much stress on the great necessity of perfecting well this part of the operation; for, upon a proper and free denudation of the fistulous orifice, success or failure will mainly depend.

Sometimes one edge of the fistula is thinner than another. Velpeau and others have noticed this fact, but in not a single instance have I found (as they did) the thinner edge behind and the thicker before. Where there was any appreciable difference, the reverse was the fact in every case that I have as yet examined. This thinning of the anterior edge, where it was right at the neck

of the bladder, was always a serious obstacle to the proper closure of the fistula. By giving way too soon, it almost invariably left an opening at the point of its greatest thinning. This, however, is a peculiarity belonging to individual cases, and will be dwelt on more particularly when we come to describe them.

Fig. 6.



Of the Suture Apparatus.—Sutures all serve the same general purpose, viz. the bringing and holding together parts that we wish to unite. They are variously named, according to circumstances—as the Interrupted, because it is solitary; the Continued, because a plurality of them are joined together; the Quilled, be-

cause of the peculiar method of securing it; and the Twisted, for a similar reason.

The one that I use for closing vesico-vaginal fistulæ, I have termed the clamp suture, from its peculiar method of action. Thus, if the profession allow me to introduce a new suture by its most appropriate name, we shall then have in general use, sutures named, first, according to their relation, the interrupted and continued. Second, according to the method of securing them, the quilled and twisted; and third, according to its method of action, the clamp suture.

As all sutures are but modifications, one of another, so is the clamp a modification of the quilled.

The clamp suture is composed of small annealed silver wire fastened to cross-bars, after the manner of the quilled suture. The wire is drawn down to about the size of a horse-hair, and then annealed. The cross-bars, or clamps, are very small, not more than a line in diameter, and made of silver or lead, as most convenient. If of silver, they may be tubular; when of lead, solid. They must be highly polished, and without the slightest asperity, particularly at their extremities. They act as clamps in this way. The parts embraced between them, being held in close apposition, swell upward, and overlap them; while they, by pressure, produce an ulceration in the vaginal surface, sufficient to allow of their being perfectly embedded, and after a while even sometimes hidden from view. This ulcerative process is attended, of course, with a purulent discharge, which, continuing for three or four days, diminishes, and soon ceases altogether; but not till the bed made by the clamp becomes (p. 70) lined with mucuous membrane. After this the apparatus would lie innocuously in the tissue for an indefinite period. I have allowed it to remain long enough for the extremities of the clamps to be covered over completely by firm granulations, which, opposing considerable resistance to their removal, had to be lacerated before this could be accomplished.

This suture is far preferable to anything before suggested for the purpose. Its introduction dates from June 1849, since which time I have had comparatively little trouble in the treatment of

the great majority of cases of vesico-vaginal fistula. Properly applied, this suture never ulcerates out, having always to be removed by means of scissors, hooks, and forceps. It may be allowed to remain intact for six, eight, or ten days, or even longer. If removed too soon, the delicate cicatrix may gradually yield to the traction of the ascending uterus, or to the force exerted by the bladder in expelling its contents, and thus reproduce a small fistulous orifice to be closed by a subsequent and more cautious operation. I have seen the new cicatrix give way from another cause, and perhaps it is the chief one. The clamps, burrowing in the vaginal surface, leave a deep sulcus or fissure on each side of the new cicatrix, which, when they are removed too soon, fill up by granulation. It is a law of all granulating wounds to contract as they heal, and this contraction on each side of the new cicatrix is often sufficient to pull it gradually apart. But if the clamps are allowed to remain till their sulci are covered with mucous membrane, then there is no danger of this accident, for these chasms then gradually disappear, less by filling up with granulations, than by an absorption of their elevated edges.

Accidents of this sort have happened repeatedly in my hands, from a too early removal of the suture apparatus. Great judgment, which experience alone can give, is necessary to determine the length of time that the sutures ought to remain intact, for no positive rules can be laid down that will answer invariably in every case.

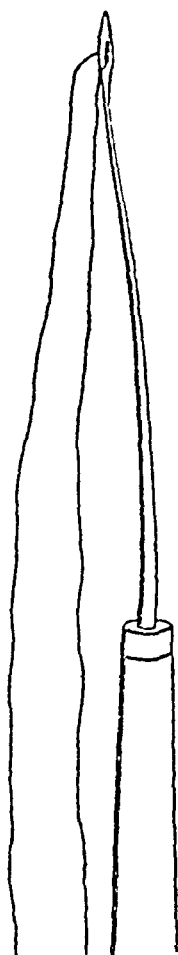
I have also seen serious mischief result from leaving the clamps too long embedded in the parts. Their burrowing and ulceration may extend entirely through the vagino-vesical structure, thereby substituting new fistulous openings for the original one. This complication is by no means incurable, but only prolongs the treatment, and postpones ultimate success.

In two or three instances I have witnessed a still more serious accident from an undue pressure of the clamps, viz. a strangulation of the enclosed fistulous edges, which unfortunately resulted in a sloughing of the tumefied parts, and consequent enlarging of the opening. In no instance, however, has this accident rendered the case hopeless, or even caused me to feel any concern either

for the immediate safety of the patient, or for ultimate success in treatment.

After the scarification is completed, the patient is allowed to rest for a few (p. 71) minutes, before the introduction of the sutures; an operation which is somewhat tedious, but not difficult.

Fig. 7.



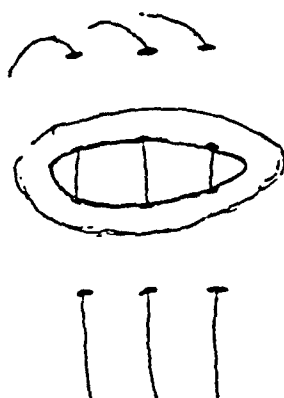
The number of sutures will depend on the size of the fistula. Less than two will not suffice for the smallest opening; while the great majority of cases will require three; and, occasionally, we meet with one sufficiently large to demand four.

The needle which I use is represented by Fig. 7. It is awl-

shaped, and spear-pointed, with the eye near the point. The shaft is about six inches long; the part near the handle is made malleable, allowing it to be bent into any desirable shape for the purpose of preventing the hand, as it grasps the handle, from obstructing the view of the operator.

To illustrate the method of suture, let us suppose a case, where the fistula is oval, transverse, occupying the *bas-fond* of the bladder, about half way between the urethra and os tinæ, in the mesial line, and large enough to admit the end of the index finger. This, in shape, size, and position, is altogether the most favourable case that can occur, both for a near performance of the operation,

Fig. 8.



and for certainty of success. Such a fistula will require three sutures.

Fig. 8 represents them introduced at proper intervals; the two outside ones passing within a fourth of an inch of the angles of the fistula. The middle one is first applied. The needle, armed with a silk thread, is entered about half an inch anterior to the scarified edge of the fistula; pushed deeply into the vesical septum, without transfixing it; brought out just at the edge of the mucous lining of the bladder; carried across the opening; made to enter the opposite side at a point corresponding with its direction anteriorly, observing the same precautions in its course; while it is brought out on the vaginal surface about half an inch beyond the scarified part.

The passage of the needle through the anterior edge of the opening is easy enough; but the loose and yielding nature of the posterior, renders some support necessary before it can be made to appear on the vaginal surface. For this purpose a blunt hook

Fig. 9.

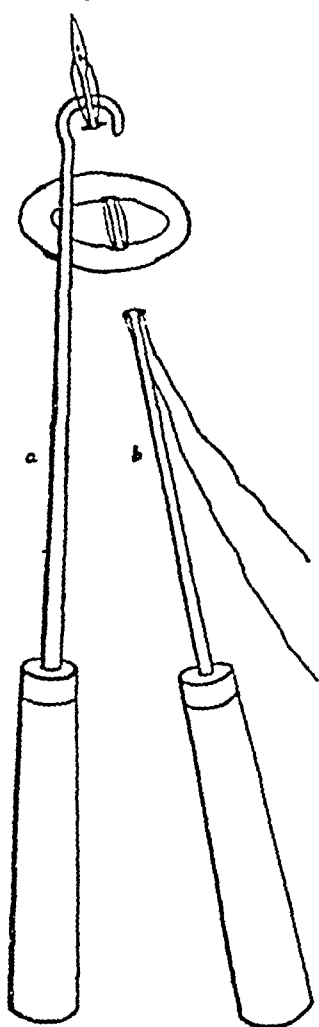
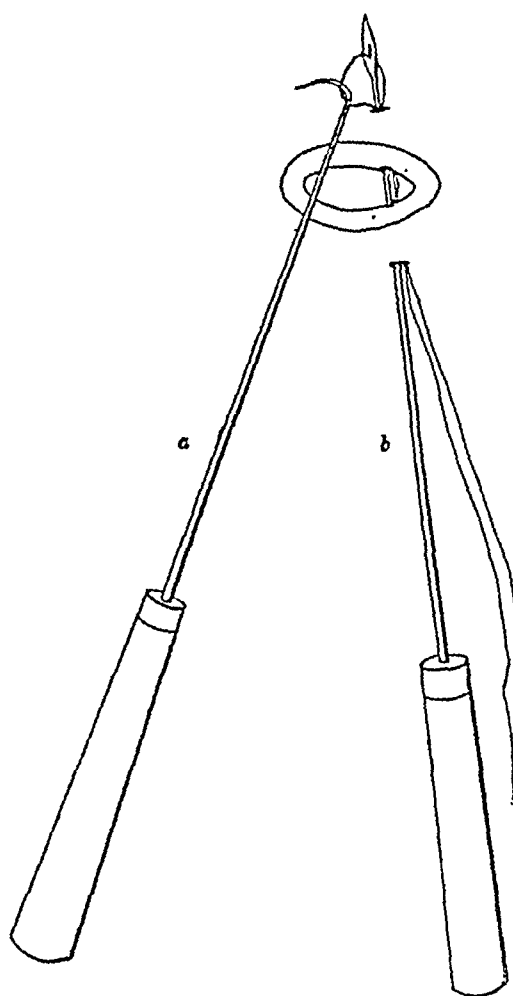


Fig. 10.



(Fig. 9, *a*) is placed flatwise, just beyond the spot at which we intend the needle to come out, thus making a fixed point for it, when it passes with great ease.

(p. 72) Fig. 9, *b*, shows the needle armed and passed as directed: the spear-point having emerged at its proper place on the distal

side of the fistula, is supported by the blunt hook, *a*, over which it rests.

As soon as this is accomplished, the blunt hook is laid aside, and a small tenaculum (Fig. 10, *a*) used to hook up the ligature which lies close by the side of the needle, *b*. There is sometimes a little delay in doing this, particularly if the parts are too contracted, or the light not good. In this case, the needle should be pushed an eighth or a fourth of an inch further on, and then retracted as much, when a little loop of ligature will be left, into which the tenaculum can be passed. (Fig. 10.) After this, the needle is to be withdrawn entirely, leaving the ligature *in situ*, with its distal end or loop securely on the hook. The hook is then drawn out, and with it, of course, the ligature, (p. 73) the two ends of which are now hanging from the vulva. The other ligatures are passed in like manner, observing the precautions already laid down.*

In pulling on the distal end of the ligature, another expedient is necessary to prevent the cutting and pain, which would inevitably attend its passage over the posterior edge of the fistula. For this, a crescent-shaped fork (Fig. 11) mounted on a shaft of convenient length, is passed up, which, pushing the ligature above its furthest point of exit, serves the purpose of a pulley; when it (the ligature) can be easily drawn backward or forward by traction on either end, without inflicting the slightest injury on the part, or pain on the patient.

Having now given directions for passing the ligatures, let us suppose that we have introduced the three, or as many as we want. The difficult part of the operation is over, and we have

* The ligatures cannot always be introduced with as little trouble as in the case just supposed. For instance, when the loss of substance is very great, the fistula is so wide that the needle cannot be made to traverse both sides of it at once; hence, it becomes necessary to hook up the ligature as soon as the needle has pierced the anterior border of the opening; when it is withdrawn, re-threaded with the distal end of the same ligature, and passed through the posterior edge. In re-threading the needle, care must be taken to pass the thread through the eye from its upper or concave surface; otherwise, when it is withdrawn, it will be found still hanging to the main thread that is stretched across the fistula, instead of slipping easily from its free end: which is a very awkward accident, inasmuch as the patient is subjected unnecessarily to the pain and delay of having it introduced again.

only to substitute the annealed silver wires for the silk ligatures; which is the work of but a few minutes. Take a piece of the wire twelve or eighteen inches long, making a small crook at one end so as to fasten it securely to one of the ligatures. Fig. 12 shows the

Fig. 11.

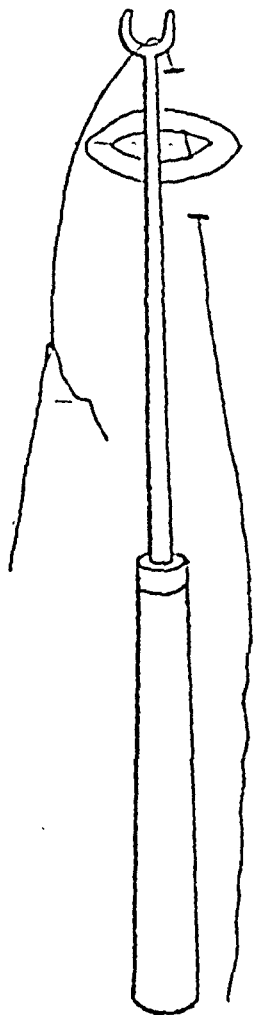
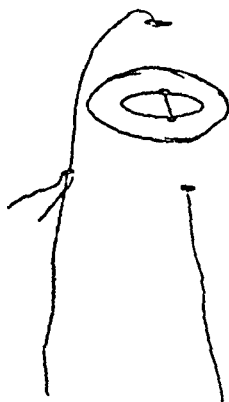


Fig. 12.



wire crooked and hanging to the end of the thread; the other end of the thread being pulled on till it comes out, leaving the wire in its place. In the same way we replace the remaining silk ligatures with silver wire; both (p. 74) ends of which project from

the vulva, the proximal directed downward, and the distal held upward.

The next step is to secure them by means of the clamps. In Fig. 13 the wires were represented passed, the two ends of each

Fig. 13.

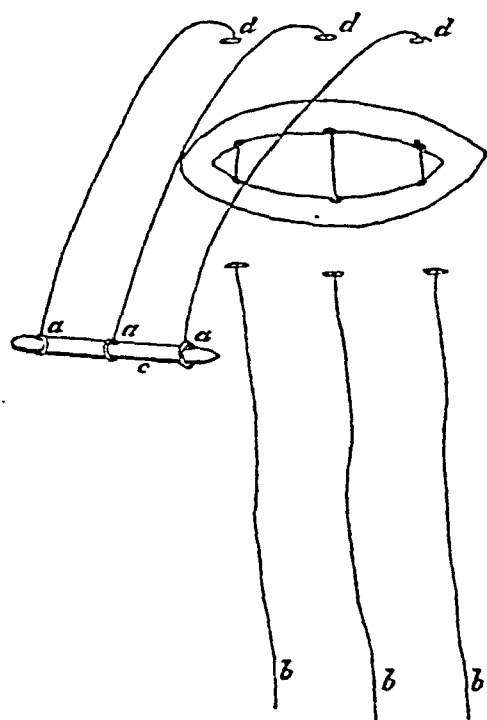
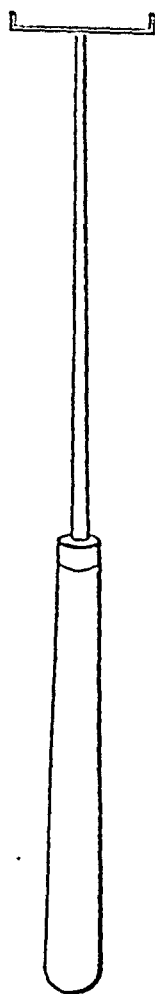


Fig. 14.



brought out of the vulva; the distal *a, a, a*, to the left; the proximal *b, b, b*, to the right. The distal ends are passed through small oblong holes made in the silver or leaden bar *c*, to suit the distances between the points of suture at *d, d, d*. The wires may be fastened to the bar or clamp *c*, by being turned twice around it,

or by being passed through a perforated shot and bent over it. This done, we now pull upon the proximal ends *b b b*, and, as a matter of course, the bar *c* is carried into the vagina, up above the fistula, and made to occupy a bed right over the orifices *d d d*. Here, the crescent-shaped fork is supplanted by a modification of it, Fig. 14, broad enough to serve the purpose of a pulley for all three of the wires. The next step is to pass another bar or clamp on the (p. 75) proximal ends of the wires, and to push it along them into the vagina, till it occupies a position in front of the fistula, corresponding exactly with the one behind it.

Fig. 15.

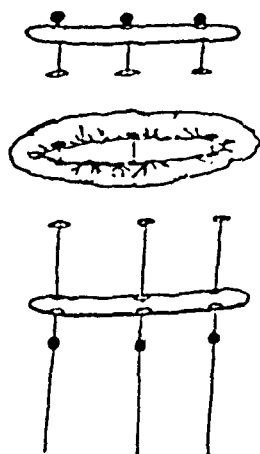


Fig. 16.



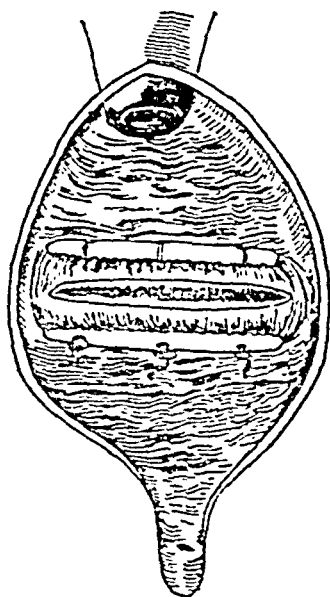
Fig. 15 shows the two clamps, one on each side of the fistula, and everything ready for closing it. The proximal clamp is pushed up by the crescent-shaped fork, while the wires are held firmly. This brings the denuded edges of the fistula into such close contact that it would be difficult to enter a common sized probe between them. The force necessary for tightening the clamps will depend upon the judgment of the operator; not enough will allow the parts to gape, while too much, which is the most frequent fault, will produce the bad effects formerly alluded to.

A simple and perfect contrivance now serves to hold the clamps in their proper places. A small bird shot, perforated, is passed

along each wire close against the proximal clamp; when, the wires being held securely, they are gently but firmly compressed by means of a long strong pair of forceps (Fig. 16), whereby they are made to perform the office of a knot in preventing the clamp from slipping off the wire. The wires are cut off about a fourth or eighth of an inch from the shot, and then bent over, which effectually prevents their slipping off.

Fig. 17 shows the appearance of the fistula and suture apparatus after the (p. 76) operation; the edges of the opening in apposi-

Fig. 17.



tion; a clamp on each side of it; the flattened shot against the proximal clamp; the wires cut off and bent over the shot, which protects the recto-vaginal surface against their sharp ends, as well as prevents their slipping.

The operation, which may have lasted some twenty or thirty minutes, or, under any circumstances, not more than an hour, is now over; and our patient is ready for bed, complaining only of fatigue from the constrained position.

There is one peculiarity about the instruments, which greatly facilitates the operation. For instance, the tenaculum, the

needle, the blunt hook, and the crescent-shaped fork, have their shafts made malleable, so that they may be bent in a direction to keep the hand of the operator below the axis of the vaginal canal, which preserves the line of vision unobstructed.

Of the Catheter.—Surgeons have always felt that something more was necessary to cure a case of vesico-vaginal fistula, than merely closing it mechanically. The urine has been the great cause of failure. To prevent its percolation through the closed opening has been regarded, heretofore, as almost insuperable. The catheter was tried by all, but its frequent introduction had a direct tendency to disturb the healing process, and to hasten the mischief it was intended to obviate; while all attempts to secure it permanently in the bladder by any external contrivance has proved abortive.

Desault used a large gum-elastic catheter, "fixed to an apparatus resembling a truss, by means of a movable silver plate, provided with an aperture for its removal." Tying it to the hairs of the vulva, and other equally useless expedients have been resorted to.

According to Chelius, the operation of paracentesis vesicæ was practiced by Wutzer, who, he says, had the greatest success in the treatment of this disease, having cured three cases out of eighteen. He compliments the efforts of his countryman by saying, "That he has importantly contributed to perfecting the operation, and, by the addition of paracentesis vesicæ, in order more completely to draw off the urine, has advanced considerably farther than his predecessors."

Wutzer gives specific directions for puncturing the bladder above the pubes: after which a tube is to be introduced, and "fixed immovably by means of wing screws in the cleft of a previously well fitted belly girdle, after which, the patient should be carefully conveyed to a bed previously prepared, *placed on her belly, upon suitably cut out leather cushions, and properly buckled in it with suitable leather straps.*" I allude to this method by Wutzer, merely to show what desperate efforts have been made to prevent the urine from escaping through the fistula during the process of treatment.

With me, as with others, this has been the most serious obstacle to the success of the operation; for, if a single drop of urine finds its way through the (p. 77) fistulous orifice, it is sure to be followed by more, and thus a failure to some extent is almost inevitable.

Knowing that something to draw off the urine continually was absolutely indispensable to success, and seeing that all other operators had failed to secure a catheter in the bladder by any justifiable external means, I conceived the idea of contriving for this purpose, a self-retaining instrument. A sponge tent was the first thing suggested to my mind. I supposed, if a long narrow piece of sponge could be safely introduced into the bladder, that it would absorb the urine as fast as secreted, which, by capillary attraction, would pass along the sponge, and escape without coming in contact with the fistula. Accordingly, a piece of fine sponge some three or four inches long, narrow in the middle, larger at each end, with a strong silk thread passing through its whole length to prevent its being torn, or broken, was first used. (Fig. 18.) Concealed in a bi-valve catheter, it was readily introduced, the middle portion *c*, enveloped in gold beater's skin lying in the urethra, the small flat end *a*, occupying the cavity of the bladder, while the larger extremity *b*, hung out between the labia. It acted the part of a syphon admirably, every drop of urine passing through it; but unfortunately for my patients (two of whom were experimented on with it), it became encrusted and perfectly saturated with calculous deposits, rendering its removal painful, difficult, and even dangerous. This expedient, promising so much in theory, and performing so ill in practice, was necessarily abandoned.

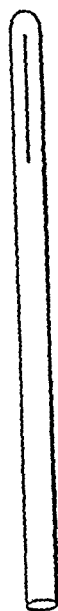
Following up the idea of a self-retaining apparatus, I next hit upon the following contrivance. I took a piece of gum-elastic bougie (No. 5 or 6), some four or five inches long, and made a longitudinal split an inch long entirely through it, beginning about a fourth of an inch below the rounded end. (Fig. 19.) A piece of silver wire, a little longer than the catheter, was passed along it and fastened neatly at its vesical or split extremity. Traction on the lower end of the wire caused the sides of the split

to open (Fig. 20), which allowed the urine to pass off freely, while the bulbing at *a a* held it securely in the bladder. This seemed, at first, to promise success, but after trying it in various cases for about twelve months, it, like its predecessor the sponge, had to be laid aside. There were several (p. 78) reasons for its failure. If made of a larger catheter than a No. 5 or 6, it would not open and close with regularity, and hence, would press unequally and injuriously on the fistula; whereas, when made of a No. 5 or 6,

Fig. 18.



Fig. 19.



its calibre was not large enough to permit a free discharge of the mucopurulent secretion which always attends the use of silken sutures; and this compelled its removal, at least two or three times a day, for the purpose of cleaning it out. Hence, its frequent introduction, with the consequent disturbance to the parts from the opening and shutting of the split end, interfered with the healing process to such an extent as to make it necessary to give up its use, entirely.

Foiled in this, I devised another instrument on the self-retaining principle. It was a large silver catheter, curved in opposite

Fig. 20.

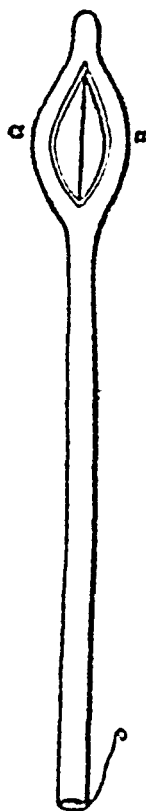
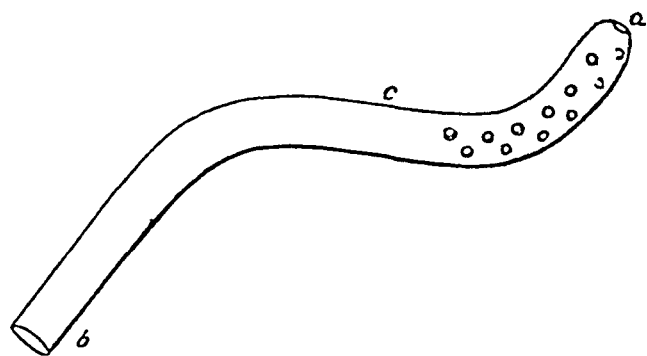


Fig. 21.



directions, giving it a sigmoid form (Fig. 21). The end *a* was carried up behind the symphysis pubis, the part *c* lay in the urethra, while the extremity *b* hung down between the nates.

This was the first successful approximation to what was really wanted. When the patient lay on the back, the end *b* was lower than the base of the bladder, which made it literally a syphon; when she turned on either side, it had a semi-rotation that still kept the end *a* upward, while the outer extremity hung downward over the thigh, inviting the easy passage of the urine.

To insure a free discharge of the muco-purulent secretion along with the urine, I made a long narrow slit on each side instead of the holes, as here represented. To see how the instrument would answer, I introduced it into the bladder of a patient having a very large fistula. Feeling well satisfied with its performance, I attempted to remove it and found (p. 79) it impossible to do so. Folds of mucous membrane had projected into the fenestra, and thus locked it up in the bladder: they were disengaged by the finger passed up through the fistula. The two long openings were then closed and several round ones made, about the size of those represented. They were larger than in ordinary catheters, on account of the abundant tenacious secretion before alluded to.

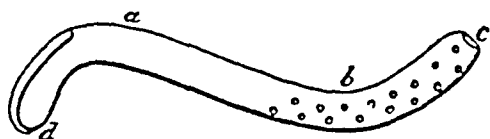
I operated on a case, and applied what I then supposed to be a faultless instrument. Everything progressed well for five or six days, the catheter remaining in the bladder intact for that length of time; but now it became necessary to remove it for the purpose of cleaning out the mucus and urinary concretions that were obstructing the free egress of the water. But here I was foiled. I could pull it down for, perhaps, an inch, when it suddenly stopped; then by letting it go, it would slip back into the bladder with a sort of jerk. It evidently seemed to be fastened there by some means that I could not exactly comprehend. Every reasonable effort to remove it proving abortive, I, at last, pulled it out by main force. On its removal, the secret of its retention was explained by the shreds of mucous membrane (some an inch long) hanging from each orifice on the under and lateral surfaces of the catheter. The long-continued presence of an instrument in the urethra, which was entirely too large for it, irritated and inflamed the lining membrane, and caused it to throw out granulations. These, with the granulations of the fistula, shot little granules through the holes in the catheter,

which spread out into button-shaped knobs on its inner surface, thereby preventing its removal. The injury done to the part, and the pain inflicted on the patient, may very well be imagined.

This instrument was variously modified (always keeping in view the self-retaining principle); but it was not reduced to its present simple form until about three years after this. I will not detain the reader longer with a statement of the troubles and disappointments that were encountered before I got it perfected, particularly as it will be necessary, in giving the history of individual cases, to speak of these amongst the causes of failure in some of the operations.

The urethra in some women is less than an inch long, while in others it may be an inch and a half; besides, it may be so small in some, that a No. 5 catheter is as large as can be borne with any

Fig. 22.



degree of comfort, while others will take a No. 9 or 10, and retain it easier than one smaller. Thus, it is evident, that almost every case may require its own catheter, peculiar in length, diameter, and curvature.

Fig. 22 is a correct representation of the self-retaining catheter, and exactly of the size and shape that is most generally required. It may sometimes be curved a little more. The end *c* is introduced and lodged up behind the symphysis pubis; the part from *a* to *b* lies in the urethra; while the outer extremity *d*, hangs down immediately below the meatus urinarius; this downward projection at *d* serves the double purpose of preventing it from slipping (p. 80) into the bladder, and of preserving its parallelism. If this part is too straight, running in the direction of the axis of the main channel from *a* to *b*, the instrument, after a few hours' use, will revolve on its own axis, and the end *c* may be turned to one side, or even so far round as to impinge on the fistulous opening. Should this accident happen, the instrument is not well suited to

the case. It is either too long, too short, too crooked; or, what is more likely, not curved down enough below the meatus.

When well fitted to the case, it can be worn with great ease to the patient; and never turns, nor slips out, it matters not whether she lies on the back or side. It is perfectly self-retaining, being held in the bladder by an internal pressure against the symphysis pubis, and by an external pressure on the outer end exerted by the labia overlappping it, and hiding it entirely from view. The holes should be small, about as represented in the drawing.

Thus, I have, as briefly as possible, described the mechanical apparatus absolutely necessary for the successful treatment of vesico-vaginal fistula.

Of the After-Treatment.—The operation finished, the patient is placed in bed, and the catheter introduced into the bladder. A moment will suffice to show the urine leaking from its outer extremity.

A large anodyne should now be given, such as morphia, laudanum, paregoric, or whatever we may know will best agree with the patient. The bowels are to be kept perfectly quiescent, till the success or failure of the operation is ascertained. I have often kept them locked up for three and four weeks without any bad consequences whatever to the general system. In but two instances, that I recollect, have I ever permitted them to be opened under ten or fifteen days from the time of the operation. This is very easily done. Previously to the operation some light laxative medicine must be given: after it, the diet must be of a constipating character. I generally direct my patients to live on tea and crackers, allowing coffee if preferred, and prohibiting meats, fruits, saccharine substances, and all articles of food made of Indian, or common corn meal. Formerly, I allowed as little water as possible; but latterly, since the introduction of silver sutures, and the perfection of the catheter, I have not thought its interdiction necessary. To assist the diet in producing constipation I order some form of opium in as large doses as can be borne, at least twice in the twenty-four hours. Old fistula cases are generally used to opium; and where they are not, they soon learn its beneficial effects. It calms the nerves, inspires hope, relieves

the (p. 81) scalding of the urine, prevents a craving for food, produces constipation, subdues inflammatory action, and assists the patient, doomed to a fortnight's horizontal position, to pass the time with pleasant dreams, and delightful sensations, instead of painful forebodings, and intolerable sufferings.

There is not the least necessity for the patient's assuming the erect posture, even for a moment: thus, by diet, opiates, and quietude, a perfect state of constipation can be kept up as long as we could possibly want it in any case. All this facilitates the healing process, which is effected by the "first intention;" or, if it fail, it does so only at one or two points, which may be subsequently closed.

The catheter is to be removed as often as necessary to keep it clear of concretions and mucus, which, in a few cases, may be twice a day; in some, once; while in others, it may be allowed to remain two or three days, or even longer. It is to be carefully watched, and must not be permitted to remain long enough to become obstructed. I have seen a failure result from a neglect of this precaution.

The patient's comfort is greatly promoted, by washing the vulval opening twice a day, or oftener, with warm or cold water, as may be preferred.

For this purpose a common bed-pan is placed under the nates, as she lies on the back: when the water may be thrown into the os externum, over the mons, vulva, and inguinal regions, by means of a syringe holding some six or eight ounces. The water has sometimes to be thrown with considerable force to remove the urinary deposits from the nates and genitals.

The patient may lie on the back, or on either side, changing her position whenever she pleases; but in no instance is she allowed to raise up in bed.

Some women are more cleanly than others in protecting themselves and clothing from the urine. Most of them prefer old cloths to absorb it, which are changed as frequently as necessary for comfort.

On the third or fourth day after the operation, I usually examine the sutures to see if all is right. This must be done with

as little exertion on the part of the patient as possible. On the sixth or seventh, I examine them again, and if they are doing no mischief, it is much better not to remove them till the ninth or tenth day. The removal of the clamps is occasionally troublesome, but by a little care it can be done with sufficient ease to both patient and operator. The flattened shots are first clipped off, then by a blunt hook, the anterior clamp is readily elevated from its bed and removed; after which, the posterior one, with the wires attached, may be hooked up, pushed backwards, disengaged entirely, and then lifted out with the forceps.

This accomplished, place the patient in bed again, and continue the use of the catheter, with the recumbent position, for several days longer, to prevent any strain or traction on the delicate new cicatrix.

By allowing the patient to get up too soon, and evacuate the contents of the bladder spontaneously, there is danger of rupturing the cicatrix, but by persevering with the catheter and position, till it has time to become well organized, (p. 82) there is no danger. This will take usually fifteen days from the performance of the operation.

In other parts of the body, most surgeons have witnessed the sudden disruption or gradual yielding of a freshly cicatrized wound, which had been submitted to undue motion, or too strong distention. A case of this kind recently occurred in my practice. A negro woman (aged 27) had a small tumour on the dorsal aspect of the right thumb, involving the skin. It was removed by two transverse elliptical incisions; the edges of the wound were brought together and dressed with collodion, while the thumb was bandaged to a straight splint to prevent any motion in the joint or traction on the cicatrizing wound. It healed by the first intention; the dressings were removed on the seventh day, but the splint was continued on the palmar aspect of the thumb for seven days longer. It was then laid aside, as I supposed the cicatrix to be strong enough to resist the flexure of the thumb. Everything went on well for three or four days longer, when the patient, who was a cook, suddenly lifting a boiling pot from the fire, was alarmed by the snapping asunder of the cicatrix on

the back of the thumb, which made a noise so loud as to be heard all over the room. The cicatrix had burst open through its whole extent; the blood flowed freely and the woman was greatly frightened. It was dressed precisely as before; it healed up as kindly; and by preserving the same precautions for a longer time, the cicatrix remained permanently organized, the skin in the neighbourhood yielding, and accommodating itself to the motions of the thumb as perfectly as it ever did before any loss of tissue. If such an accident as this can occur after eighteen days of cicatrizing, we need not be surprised at the gradual or sudden yielding of a cicatrix in the vagino-vesical structure in a shorter space of time.

I have now completed what I have to say in a general way on the subject of the operation for vesico-vaginal fistula. It remains to detail individual cases, which will prove the curability of the disease, and also illustrate the varieties and complications to which it may be liable. The cases that occurred to me early and which were given to me for the sake of experiment, will show the difficulties that had to be overcome, the many disappointments that had to be borne, and the ultimate success that crowned my efforts after the perfection of the mechanical contrivances; which, as it will be seen, was the work not of a day, and the result, not of accident, but of long, laborious and persevering application.

But this communication has already reached to such an extent that I must postpone the relation of my cases to a future opportunity.

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ROBERT KOCH

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Robert Koch

BIOGRAPHY

- 1843 Born December 11, in Klausthal, the son of a mining official of Hanover, the third of thirteen children. Attended the Gymnasium of his native town.
- 1862 Age 19. Began his medical studies at Göttingen where he was influenced by the teachings of Jacob Henle.
- 1866 Age 23. Received the M.D. degree. Interned at the Hamburg General Hospital.
- 1869 Age 26. Started practice in Rakwitz in Posen.
- 1870 Age 27. Volunteered for medical service during the Franco-Prussian War.
- 1872 Age 29. Started practice in the town of Wollstein in the District of Bomst in Polish Prussia; soon became District Physician.
- 1876 Age 33. Demonstrated the complete life cycle and sporulation of the anthrax bacillus and demonstrated for the first time a specific microorganism as the cause of a definite disease. Devised and developed many ingenious methods of isolating, mounting and staining bacteria.
- 1880 Age 37. Made a member of the Imperial Board of Health by the German Government in recognition of the value of his work. This enabled him to give up his country practice and devote his time to research.
- 1881 Age 38. Introduced steam sterilization as more efficient than the chemical sterilization advocated by Lister.
- 1882 Age 39. Announced his discovery of the bacillus of tuberculosis.

- 1883 Age 40. As head of the German Cholera Commission, visited Egypt and India. Discovered the cholera vibrio. For his discovery of the bacillus of infectious conjunctivitis, received 100,000 marks from the Prussian State.
- 1885 Age 42. Appointed professor of hygiene and bacteriology at the University of Berlin.
- 1890 Age 47. Introduced old tuberculin.
- 1891 Age 48. Director of the Institute for Infectious Diseases at its founding in Berlin.
- 1896 Age 53. Investigated Rinderpest in South Africa at the request of the English government. Studied Texas fever, black-water fever, tropical malaria and plague.
- 1897 Age 54. Produced new tuberculin.
- 1898 Age 55. Studied malarial fever in Italy.
- 1902 Age 59. Studied Rhodesian red-water fever, horse-sickness, trypanosomiasis and recurrent fever in German East Africa.
- 1905 Age 62. Received the Nobel Prize.
- 1906 Age 63. Studied sleeping sickness in Africa.
- 1910 Age 67. Died on May 27, of "heart failure." Koch's body was cremated by his own wishes and the ashes placed in the Berlin Institute for Infectious Diseases.

In appearance, Koch was a typical German savant of Prussian cast, in character dignified, modest and fair-minded, altogether one of the greatest men of science his country has produced. (Garrison)

EPONYMS

BACILLUS: The *Bacillus tuberculosis*.

BACILLUS: The Koch-Weeks' bacillus—found in acute infectious conjunctivitis or Egyptian ophthalmia.

LAW OR POSTULATES OR CIRCUIT: The specificity of a microorganism is not demonstrated without the fulfilment of the following conditions: (1) The microorganism is present and discoverable in every case of the disease; (2) it is to be cultivated

in a pure culture; (3) inoculation from such culture must reproduce the disease in susceptible animals; (4) it must be re-obtained from such animals and again grown in a pure culture. (Dorland)

LYMPH: See tuberculin.

PHENOMENON: the sudden collapse of tuberculous animals when a fresh culture of tubercle bacilli is injected within the peritoneum. The exudate that forms contains lymphocytes almost exclusively. (Dorland)

REACTION: The tuberculin reaction.

SPIROCHETA KOCHI: A species found in cases of East Africa tick fever.

STAIN: Koch-Ehrlich's stain or solution; consists of 100 parts of a filtered aqueous solution of anilin oil, 10 parts of absolute alcohol, and 11 parts of a concentrated alcoholic solution of fuchsin, methylene blue or gentian violet.

STREPTOCOCCUS KOCHI: A species from rabbits with artificial septicemia.

TUBERCULIN: New; called also bacillen emulsion, emulsio bacilli and tuberculin B. E. A form of tuberculin consisting of a suspension of pulverized bacilli in water to which an equal quantity of glycerin has been added.

TUBERCULIN: Old; the concentrated germ-free culture-medium on which tubercle bacilli have been grown, then killed by heat and filtered; the filtrate is concentrated by evaporation to one-tenth of its volume.

INTRODUCTION

Robert Koch must have been born with unmeasurable ambition and energy and an inspiration for solving scientific problems. His childhood seems to have been an ordinary one except that he was the third of thirteen children. In 1862, at the age of nineteen, he began his medical studies at Göttingen where he was influenced by the teaching of Jacob Henle who had proposed a theory of contagion in 1840. Many people believed that Henle's influence lead Koch to his researches in bacteriology. After

receiving his medical degree Koch interned at the Hamburg General Hospital and then started in medical practice. Koch interrupted his practice by volunteering for medical service during the Franco-Prussian War.

In 1872, at the age of twenty-nine, Koch finally settled down to a medical practice in the town of Wollstein in the district of Bomst in Polish Prussia. This town had a population of 4,000 people but Koch soon obtained the position of District Physician so that his practice covered a large territory. In spite of long hours of office practice and traveling into the outlying district, Koch found and took time to carry on original research. At the end of the room in which he received patients he rigged up a small laboratory behind a curtain, provided himself with a microscope and a few other necessities, and started to work. The first subject which drew his interest was the problem of an epidemic of fever attacking the cattle of the region and endangering the human population. Koch obtained some of the infected blood from these animals and injected it into mice. By repeated examination with his microscope he saw that the bacteria in the sick mice grew into long threads and changed under favorable conditions into forms with spores. The bacteria were fairly easily killed by sterilization but Koch found the spores resisted death in a remarkable degree. Even after a long period of adverse conditions, the spores were able to change themselves into an active form and to transmit the disease to healthy animals.

Meanwhile, Ferdinand Cohn, Professor of Botany at Breslau, was working with bacteria and had discovered that certain types had the ability to form spores. Koch wrote to Cohn, telling him of his findings and offered to demonstrate them. Cohn gladly invited Koch to demonstrate the specimens before a group of scientists, including Cohnheim, Weigert and Truabe, at the Botanical Institute. There Koch's experiments and conclusions were enthusiastically received. Koch had proved the life cycle of the anthrax bacillus and demonstrated for the first time a specific microorganism as the cause of a definite disease. See the following pages for Koch's paper on the anthrax bacillus which is here reproduced in its entirety.

For the next few years Koch busied himself in improving methods of studying bacteria. He developed by his own ingenuity several methods of isolating, mounting and staining organisms to be examined under the microscope. He also worked assiduously with the photography of microorganisms. During this same period he introduced steam sterilization as more efficient than the use of chemicals which had been popularized by Lister. Other important work of Koch was the use of solid media for growing bacteria in pure culture. Koch demonstrated methods of bacterial isolation and culture before the International Congress of Medicine held in London in 1891 and the great Pasteur, as the leader of the bacteriologists, recognized the importance of Koch's work and praised him highly.

In 1880 Koch's work was recognized by the German Government and he was made a member of the Imperial Board of Health, thus relieving him of the necessity of carrying on his small country practice.

On March 24th, 1882, at a meeting of the Berlin Physiological Society, Koch announced the discovery of the bacillus of tuberculosis. This work is the greatest and best known of all of Koch's labors. The organism requires a special media and proper conditions for its growth in culture and a unique staining method for its observance. In contrast to the difficulty of staining and growing the organism, Koch showed that, after it was injected into certain laboratory animals, tuberculosis was readily produced. Koch then formulated the postulates or law which has ever since been known by his name. (See eponyms.) For this work, in the face of the teaching of the day that tuberculosis was the result of nutritional disturbances, Koch took his place as the greatest bacteriologist of his day and as one of the great physicians of all time. By the discovery of the actual cause of tuberculosis real scientific progress was possible toward controlling this widespread and terrible affliction. For this discovery of the bacillus of tuberculosis, Robert Koch received the Nobel Prize in 1905. Koch's paper of 1882 announcing the discovery of the bacillus of tuberculosis is included in this number.

BIBLIOGRAPHY OF WRITINGS

A. Army Medical Library.

B. New York State Library.

C. New York Academy of Medicine Library.

D. Kings County Medical Society, Brooklyn, Library.

E. Lane Medical Library of Stanford University.

F. John Crerar Library, Chicago.

1. Ueber das Vorkommen von Ganglienzellen an den Nerven des Uterus. Eine von der medicinischen Fakultät zu Göttingen gekrönte Preisschrift. (On the presence of ganglion cells on the nerves of the uterus. A prize paper to the Medical Faculty of Göttingen.) Göttingen, Kaestner, 1865. 4°, 19 pp., 3 pl. In A., F.
2. Die Aetiologie der Milzbrandkrankheit, begründet auf die Entwicklungsgeschichte des Bacillus Anthracis (1876). (The etiology of anthrax based on the developmental history of the anthrax bacillus.) Beitr. z. Biol. d. Pflanz., 2: 277-310, 1877. Also: Mitth. a. d. k. Gesundheitsamte., 1: 49-79, 1881. Also No. 9 of Klassiker der Medizin, Sudhoff, Leipzig, Barth, 1912. 12°, 47 pp., 1 p. In A, C, E, F.
3. Untersuchungen über Bacterien. VI. Verfahren zur Untersuchung, zum Conserviren und Photographiren der Bacterien. (Investigations of bacteria. VI. Procedure of research, to preserve and photograph bacteria.) Beitr. z. Biol. d. Pflanz., 2: 399-434, 1877.
4. Ueber die practische Bedeutung des Zahndurchbruchs. (On the practical significance of dentition.) Brief note before the Verhandl. aertzliche Gesellsch., 1877. Berl. klin. Woch., 14: 694 only, 1877.
5. Untersuchungen über die Aetiologie der Wundinfektionskrankheiten. (Investigations into the etiology of traumatic infective diseases.) Leipzig, Vogel, 1878. 8°, 80 pp., 5 pl. In A, C, D, F. Also, trans. by W. W. Cheyne. London, New Sydenham Soc., 1880. 8°, xiii, 74 pp., 5 pl. In A, C, D, E, F.

6. Zur Lehre von den Gelenk neuralgien. (On the warning of joint neuralgia.) Brief note before the Congr. d. deut. Gesellsch. f. Chir. Berl. klin. Woch., 15: 356-357, 1878.
7. Fehlen der Milz. (Absence of the spleen.) Ibid., 16: 81-82, 1879.
8. Über Aphasie auf anämischen Boden. (Aphasia on an anemic basis.) Ibid., 105-107, 1879.
9. Über die Wirkung der Oxalate auf den thierischen Organismus. (On the effect of oxalate on the animal organism.) Dorpat, 1879. 8°. Also: Arch. f. exper. Path. u. Pharmacol., 14: 153-199, 1881.
10. Ein zweiter Fall von Aphasie ex Anämia. (A second case of aphasia due to anemia.) Berl. klin. Woch., 17: 229-230, 1880.
11. Die Frage der Curpfuscherei. (The question of quackery.) Aerztl. Int.-Bl., München, 27: 295; 309, 1880.
12. Zur Untersuchung von pathogenen Organismen. (The investigation of pathogenic organisms.) Mitth. a. d. k. Gesundheit., 1: 1-48, 14 pl., 1881. Also, trans. By V. Horsley, in W. W. Cheyne's Recent essays on bacteria. London, 1886, pp. 3-64. In A, B, C, D.
13. Untersuchungen über die Desinfection mit heisser Luft. (Investigations on disinfection with hot air.) With G. Wolfhügel. Mitth. a. d. k. Gesundheit., 1: 301-321, 1881. Also, in W. W. Cheyne's recent essays on bacteria. London, 1886. pp. 519-525.
14. Über Desinfection. (On disinfection.) Mitth. a. d. k. Gesundheit., 1: 234-282, 1881. Also, trans. and abstr. by B. A. Whitelegge in W. W. Cheyne's Recent essays on bacteria. London, 1886. pp. 493-518.
15. Versuche über die Verwerthbarkeit heisser Wasserdämpfe zu Desinfectionszwecken. (Experiment on the value of steam for disinfecting purposes.) With G. Gaffky and F. Löffler. Mitth. a. d. k. Gesundheit., 1: 322-340, 1881. Also, in W. W. Cheyne's Recent essays on bacteria. London, 1886. pp. 526-533.
16. Entgegnung auf den von Dr. Grawitz in der Berliner medi-

cinischen Gesellschaft gehaltenen Vortrag über die Anpassungstheorie der Schimmelpilze. (Reply to the discourse on the adaptation theory of hyphomycetes, given to the Berlin Medical Society by Dr. Grawitz.) Berl. klin. Woch., 18: 769-774, 1881.

17. Über die Milzbrandimpfung. Eine Entgegnung auf den von Pasteur in Geuf gehaltenen Vortrag. (On inoculation for anthrax. A reply to the lecture given by Pasteur in Geuf.) Kassel. u. Berlin, Fischer, 1882. 8°, 37 pp. In A, C, F. Same, in French, Semaine méd., Paris, 2: 205; 209, 1882. Same, Kassel. u. Berlin, Fischer, 1883. 8°, 40 pp. In A. C. Same, in French, Rev. scient., Paris, 31: 65-74, 1883.
18. Die Aetiologie der Tuberculose. (The etiology of tuberculosis.) Berl. klin. Woch., 19: 221-230, 1882. Also: Berlin, 1882. 8°, 29 pp. In A. Also: Med.-Chir. Centralbl., 17: 278; 302; 326; 351; 363; 375, 1882. Also: Arch. f. Physiol., pp. 190-192, 1882. Also: Verhandl. d. Cong. f. innere Med., 1: 56-79, 1882. Also: Gior. internaz. d. sc. med., Napoli, n.s. 4: 702-716, 1882. Also: trans. by W. D. Oakley. Canada M. and S. Jour., 10: 649-655, 1882. Also: trans. by J. Eichberg. Cincinnati Lancet and Clinic, n. s. 10: 428-439, 1883. Also, with introduction by M. Kirchner, in Klassiker der Medizin, No. 19, Leipzig, Barth, 1912. 12°, 74 pp. In A, C, E, F. Also: trans. by Berna and Max Pinner. Amer. Rev. Tuber., 25: 298-323, 1932, and Nat. Tuber. Assoc., 1932. 26 cm., 48 pp., 8 illust.
19. Bericht der nach Egypten entsendeten deutschen Cholera-Commission. (Report of the German Cholera Commission in Egypt.) Mitth. d. Ver. d. Aerzte in Nied.- Oest., 9: 258-264, 1883. Also: Wien. med. Bl., 6: 1245-1250, 1883; 7: 464, 1884. Also: Allg. med. Centr.- Zeitg., 1883. Also: Wien. med. Woch., 33: 1248-1252; 1548-1551, 1883; 34: 443-446, 1884. Also: Breslau. aerztl. Zeitschr., 5: 215-218, 1883; 6: 99, 1884. Also, trans.: Med. Times and Gaz., London, 2: 447, 1883.

20. Kritische Besprechung der gegen die Bedeutung der Tuberkelbacillen gerichteten Publicationen. (Critical reply to the publications directed against the significance of the tubercle bacilli.) *Deutsche med. Woch.*, 9: 137-141, 1883. Also: Berlin, Reimer, 1883. 8°, 17 pp. In A. Also: *Allg. Wien. med. Zeitg.*, 28: 105; 119, 1883. Also: *Wien. med. Bl.*, 6: 325; 358, 1883. Also: *Oesterr. ärztl. Vereinszeitg.*, 7: 43; 51, 1883.
21. Der Seitens des—an den Staatssecretär des Innern erstattete Bericht. (The side of the—report to the State Secretary of the Innern erstattete Bericht.) *Deutsche med. Woch.*, 9: 615-617, 1883. Also: *Deutsche Vrtljschr. f. öff. Gesundths., Bruschwg.*, 16: 493-515, 1884.
22. Die Aetiologie der Tuberculose. (The etiology of tuberculosis.) *Mitth. a. d. k. Gesundheit.*, 2: 1-88, 10 pl., 1884. Also, trans. and abstr.: *Phila. Med. Times*, 14: 542-545, 1884. Also, trans. by S. Boyd, in W. W. Cheyne's recent essays on bacteria. London, 1886. pp. 67-201. Also, trans. by F. Saure: *Amer. Vet. Rev.*, 13: 54-82; 104-130; 148-171; 197-214, 1889, and New York, Jenkins, 1890. 8°, 97 pp. In C. Also: *New York Journal and Advertiser*, 1901, and New York, 1901, 8°, 10 pp., 11. In A, C.
23. Experimentelle Studien über die künstliche Abschwächung der Milzbrandbacillen und Milzbrandinfection durch Fütterung. With Gaffky and Loeffler. (Experimental studies on the artificial attenuation of the anthrax bacillus and infection with anthrax through fodder.) *Mitth. a. d. k. Gesundheit.*, 2: 147-181, 1884.
24. Die Beziehungen der Tuberkelbacillen zur Aetiologie der Tuberkulose. (Relations of the tubercle bacillus to the etiology of tuberculosis.) *Med.-Chir. Centralbl.*, 19: 50, 1884.
25. Discussion on Conferenz zur Erörterung der Cholerafrage. (Discussion on conference for debate of the cholera question.) *Berl. klin. Woch.*, 21: 478-483, 1884. Also, transl. by G. L. Laycock in W. W. Cheyne's Recent essays on bacteria. London, 1886, pp. 327-384. Also, transl.: *Brit. M. J.*, 1: 6; 62, 1886.

26. Ueber die Cholera mit besonderer Rücksicht auf die Comma-bacillen. (On cholera, with special reference to the comma bacillus.) Wien. med. Bl., 7: 991; 1023; 1062; 1094, 1884.
27. Ueber die Entstehungsursache der asiatischen Cholera. (On the source of Asiatic cholera.) Med.-Chir. Centralbl., 19: 424, 1884.
28. Il Cholera. Gazz. Med. ital. lomb., 8 s. 6: 353; 417; 465, 1884.
29. Was wissen und können unsere Aerzte? Ueber Naturheilung und medicinische Kunst. (What do our physicians know and what can they do? On natural healing and the art of medicine.) Leipzig, Hucke, 1885. 8°. 2 Aufl. Leipzig, Hucke, 1885. 8°, 88 pp. In A, F.
30. Die Cholera auf ihren neusten Standpunkte. (Cholera from the newest point of view. Berlin, Hampel, 1886. In E.
31. Bericht über die Untersuchungen des Berliner Leitungswassers in der Zeit vom 1. Juni 1885 bis 1. Apr. 1886, ausgeführt im hygienischen Institut der Universität Berlin. (Report on the investigation of Berlin conduit water from June 1, 1885 to April 1, 1886, carried on in the Institute of Hygiene of the University of Berlin.) Berlin, Springer, 1887. 8°, 50 pp.
32. Die Bekämpfung der Infektionskrankheiten, insbesondere der Kriegsseuchen. Rede gehalten zur Feier des Stiftungstages der militärärztlichen Bildungs-Austalten am 2. August 1888. (The control of the infectious diseases, especially war epidemics. Speech given on the celebration of the founding of the Army Medical School.) Berlin, Hirschwald, 1888. 8°, 40 pp. In A, C, E. Same, rev.: Wien. Med. Bl., 11: 1306; 1371, 1888. Also: Militärarzt, Wien, 22: 177; 185; 194; 209, 1888. Also, in Russian, St. Petersburg, 1889. 8°, 100 pp. In A. (Same) La prophylaxie des maladies infectieuses dans les armées. Transl. in Rev. scient. Par., 42: 561-568, 1888.
33. Ueber bakteriologische Forschung. (Bacteriological investigation.) Wien. med. Bl., 13: 531-535, 1890. Also: Verhandl. d. X internat. med. Cong., 1890, Berl., 1: 35-47,

1891. Also: Berlin, Hirschwald, 1890. 8°, 15 pp. In A, C. Also, transl.: Brit. M. J., 2: 380-383, 1890. Also, transl. in Russian, 1890. In A. Also, transl.: On bacteriology and its results. By T. W. Hime. London, Ballière, 1890. 8°, 23 pp. In A. Also, transl.: Advances in bacteriology; an address. Wood's Med. and Surg. Monog., 9: 1-13, 1891. In A, E. Also: In Klassiker der Medizin, No. 9, Leipzig, Barth, 1912. 12°, 74 pp. In A, C, E, F.

34. Weitere Mittheilungen über ein Heilmittel gegen Tuberculose. (Further communications on a remedy for tuberculosis.) Deutsche med. Woch., 16: 1029-1032, 1890; 17: 101; 1189-1192, 1891. Also: Berl. klin. Woch., 27: 1077-1080, 1890; 28: 77-78, 1891. Also: Centralbl. f. allg. Gesundheitspflg., Bonn, 9: 385-395, 1890. Also: Heft 1-3, Berlin u Leipzig, Thieme, 1890. Also, transl.: Lancet, Lond., 2: 1085, 1890; 2: 976-979, 1891. Also, transl.: Brit. M. J., 2: 1193-1195, 1890; 1: 125-127, 1891. Also, transl.: Med. News, Phila., 57: 521-527, 1890. Also, transl.: Bull. méd., Par., 4: 1009-1012, 1890. Also, transl.: Pest. med.-chir. Presse, Budapest, 24: 1105-1111, 1890. Also, transl.: Ann. Soc. med.-chir. de Liège, 29: 446-456, 1890. Also, transl.: Med. Rec., N. Y., 38: 734, 1890; 39: 55, 1891. Also, transl.: Sicilia med., Palermo, 2: 890-896, 1890. Also, transl.: Montreal Med. St., Dec. 1890. Also, transl.: London, Heinemann, 1890. 8°, 32 pp. In A, C. Also, transl. in Swedish, 1890. In A. Also: Wien. med. Woch., 41: 1721-1724, 1891. Also, transl.: Semaine méd., Paris, 11: 17, 1891. Also, transl.: In Prof. Koch's method to cure tuberculosis popularly treated by Max Birnbaum. Milwaukee, Harper, 1891. 8°, 27 pp. Also, transl. by E. Tutzscher, Paris, Hinrichsen, 1891. 12°, 114 pp. Also: In Klassiker der Medizin, No. 19, Leipzig, Barth, 1912. 12°, 74 pp. In A, C.
35. Zur Casuistik der Bronchitis fibrinosa. (Case description of fibrinous bronchitis.) St. Petersburg. med. Woch., 9: 83-85, 1892.

36. Ueber Magenblutungen in der Gravidität. (On gastric hemorrhage in pregnancy.) Ibid., 10: 89, 1893. Also: Med.-chir. Centralbl., Wien, 28: 297, 1893.
37. Ueber das Carcinoma ventriculi ex ulcere rotundo. (On carcinoma of the stomach arising from peptic ulcer.) St. Petersburg. med. Woch., 10: 385-387, 1893. Also: Med.-chir. Centralbl., Wien, 29: 1-3, 1894.
38. Entgegnung auf den Vortrag des Herr Professor Dr. M. Schottelius: Zum mikroskopischen Nachweis von Cholera-bacillen in Dejectionen. (Reply to the lecture of Prof. Dr. M. Schottelius: On the microscopic demonstration of cholera bacilla in dejecta.) Deutsche med. Woch., 19: 739, 1893.
39. Revolverkugel in den Mund. (On gunshot wound in the mouth.) Berl. klin. Woch., 30: 246 only, 1893.
40. Ueber den augenblicklichen Stand der bakteriologischen Choleradiagnose. (The present state of bacteriological diagnosis of cholera.) Zeitschr. f. Hyg. u. Infect., 14: 319-338, 1893. Also, rev.: Berl. klin. Woch., 30: 585-586, 1893. Also: Wien. med. Bl., 16: 305; 317; 340, 1893. Also, transl.: Semaine méd., Par., 13: 265-268, 1893. Also, transl.: Med. Week., Par., 1: 265-269, 1893. Also, transl.: Practitioner, London, 51: 466-476, 1893.
41. Wasserfiltration und Cholera. (Filtration of water and cholera.) Zeitschr. f. Hyg. u. Infect., 14: 393-396, 1893. Also, crit.: Berl. klin. Woch., 30: 896-898, 1893. Also, transl. by A. J. A. Ball, London, 1893. 19 pp., fol. In A. Also: Practitioner, London, 51: 146; 218, 1893. Also: Rep. Local Gov. Bd., 1892-1893, London, 22: 439-462, 1894. Also, transl.: Semaine méd., Par., 13: 305-309, 1893.
42. Die Cholera in Deutschland während des Winters 1892 bis 1893. (Cholera in Germany during the winter of 1892-1893.) Zeitschr. f. Hyg. u. Infect., 15: 89-165, 1893. Also, crit.: Berl. klin. Woch., 30: 1103-1104, 1893. Also, transl.: Lancet, Lond., 2: 828; 891, 1893. Also, transl. by George Duncan. Edinburgh, Douglas, 1894.

8°, 150 pp. In A, F. Same, New York, Jenkins, 1895.
In D.

43. Vorlesungen über cholera. (Lecture on cholera.) Wien. med. Bl., 16: 327-329; 353; 366; 378, 1893.
44. Beobachtungen über Erysipel-Impfungen am Menschen. (Observation on the inoculation of erysipelas in man.) Zeitschr. f. Hyg. u. Infect., 23: 477-489, 1896.
45. Die Lepra-Erkrankungen im Kreise. (The course of leprosy.) Memel. klin. Jahrb., Jena, 6: 239-253, 1897.
46. Ueber neue Tuberkulinpräparate. (On new tuberculin.) Deutsche med. Woch., 23: 209-213, 1897. Also: Allg. Wien. med. Ztg., 42: 165; 177; 199; 211, 1897. Also, transl.: Méd. mod., Par., 8: 218-228, 1897. Also, transl.: Med. Week, Par., 5: 169-172, 1897. Also, transl.: Presse méd., Par., 5: 159-160, 1897. Also, transl.: Rev. de therap. med.-chir., Par., 44: 249-259, 1897. Also, transl. in Russian, Moscow, 1897. 8°, 12 pp. In A.
47. Berichte des Prof. Dr. Koch über seine in Kimberly gemachten Versuche bezüglich Bekämpfung der Rinderpest. (Dr. Koch's report on his attempt to control cattle plague in Kimberly.) (Transl. from: Agricult. J., Capetown) Centralbl. f. Bakteriolog., 1. abt., 21: 526-537, 1897.
48. Special report on researches into the cause of cattle plague. Brit. M. J., 1: 1245, 1897.
49. Aerztliche Beobachtungen in den Tropen. (Medical observations in the tropics.) Deutsche kolonial-gesellschaft. Abt. Berlin. Charlottenburg Verhandlungen, Hft. 7, 1897. Also: Berlin, Reimer, 1898. 8°, pp. 280-317. Also: Wien. med. Zeitg., 43: 381; 391, 1898. Also, transl.: Ann. d'hyg. et de méd. colon., Par., 1: 368-396, 1898. Also, transl.: Rev. scient., Par., 4. s. 10: 777; 812, 1898.
50. Reise-Berichte über Rinderpest, Bubonenpest in Indien und Afrika, Tsetse-oder Surra-krankheit, Texas-fieber, tropische Malaria, Schwarzwasserfieber. (Travel-report on cattle plague, bubonic plague, in India and Africa, tsetse or surra, Texas fever, tropical malaria, black water fever.) Berlin, Springer, 1898. 8°, 136 pp. 1 pl. In A, C.

51. Die Malaria in Deutsch-Ostafrika. (Malaria in German East Africa.) Arb. a. d. k. Gusdhtsamte, 14: 292-304, 1898.
52. Das Schwarzwasserfieber. (Black-water fever.) Ibid., 14: 304-308, 1898.
53. Ueber die Verbreitung der Bubonenpest. (On the transmission of bubonic plague.) Deutsche med. Woch., 24: 437-439, 1898. Also: München med. Woch., 44: 911-913, 1898.
54. Diagnosis, treatment and prophylaxis of tropical malaria. Transl. by E. O. Shakespeare. Philadelphia, 1898. 24°, 38 pp. In C.
55. Tropenhygiene und Tropenkrankheiten. Zweiter Bericht über die Thätigkeit der Malaria-Expedition. Aufenthalt in Niederländisch-Indien vom 21 September bis 12 December 1899. (Tropical hygiene and tropical diseases. Second report on the accomplishment of the Malaria Expedition. Stay in Dutch India from September 21 to December 12, 1899.) Deutsche med. Woch., 26: 296-297; 397-398; 541-542; 27: 88-90, 1900.
56. The study of malaria in Rome. Med. Rec., N. Y., 57: 294, 1900. Also: Riforma med., Palermo, 1: 505-506, 1900. Also: Rev. balear de Cien. méd., Palma de Mallorca, 18: 56-65, 1900.
57. Zusammenfassende Dorstellung der Ergebnisse der Malaria-expedition. (Composite presentation of the results of the Malaria Commission.) Deutsche med. Woch., 26: 781-783; 801-805, 1900.
58. Ergebnisse der vom Deutschen reich ausgesandten Malaria-expedition. (Results of the malaria expedition sent out from Germany.) Berlin, Reimer, 1900. 8°, 27 pp. In C.
59. Ueber die Bekämpfung der Tuberkulose. (On the control of tuberculosis.) Allg. Wien. med. Zeitg., 46: 360-361, 1901. Also: Deutsche med. Woch., 27: 549-554, 1901.
60. On the transference of bovine tuberculosis to man. Brit. M. J., 2: 1885-1889, 1902. Also: Vet. J., London, n.s., 7: 8-19, 1903.

61. Die Bekämpfung des Typhus. (The control of typhus.) Berlin, Hirschwald, 1903. 8°, 22 pp. Forms Heft 21 of Veröffentl. a. d. Geb. d. Mil.-San.-Wes. In A, C.
62. Die Bekämpfung der Malaria. (The control of malaria.) Zeitschr. f. Hyg. u. Infect., Leipzig, 43: 1-4, 1903.
63. Revision of Alfred Hillier's The prevention of consumption. London, Longman, 1903. 12°, 240 p., 1 pl., 1 ch.
64. Ueber die Trypanosomenkrankheiten. (On the trypanosoma diseases.) München. med. Woch., 51: 1987, 1904. Also: Deutsche med. Woch., 30: 1705-1711, 1904. Also: Berl. tierärztl. Woch., pp. 736-739, 1904. Also, transl.: Brit. M. J., 2: 1445-1449, 1904.
65. Vorläufiger Bericht über das rhodesische Rotwasser oder afrikanische Küstenfieber. (Preliminary report on Rhodesian redwater or African coast fever.) Arch. f. wissensch. u. prakt. Tierh., Berl., 30: 281-319, 1904. Also, transl.: Vet. Rec., London, 16: 507-511, 1904.
66. Ueber die Immunisierung von Rindern gegen Tuberkulose. With W. Schutz et al. (On the immunization of cattle against tuberculosis.) Arch. f. wissensch. u. prakt. Tierh., 31: 545-575, 1905. Also: Zeitschr. f. Hyg. u. Infect., 51: 300-327, 1905.
67. A few observations on relapsing fever. Med. News, 87: 1127-1129, 1905.
68. Vorläufige Mitteilungen über die Ergebnisse einer Forschungsreise nach Osafrika. 1. Recurrens. 2. Entwicklung des Piroplasma bigeminum. 3. Küstenfieber der Rinder. 4. Tsetsefliegen und Trypanosoma. (Preliminary contributions on the results of a journey of investigation to East Africa. 1. Recurrent fever. 2. Development of Piroplasma bigeminum. 3. Coast fever of cattle. 4. Tsetse flies and trypanosoma.) Deutsche med. Woch., 31: 1865-1869, 1905. Also, transl.: J. Trop. Med., 9: 43; 75; 104; 137, 1906.
69. Über den derzeitigen Stand der Tuberkulosebekämpfung. (The present state of control of tuberculosis.) Lecture at presentation of Nobel Prize. Les Prix Nobel, pp. 1-12,

1905. Also: Nord. med. Ark., Stockholm, 3. f., 5, afd. 2, No. 13, 1-13, 1905. Also: Deutsche med. Woch., 32: 89-92, 1906. Also: Zeitschr. f. Tuberk., 8: 91-100, 1906. Also, transl.: Lancet, London, 1: 1449-1451, 1906. Also, transl.: Clín. mod., Zaragoza, 5: 273-281, 1906.
70. Beiträge zur Entwicklungsbeschichte der Piroplasmen. (Contributions to the development of piroplasmus.) Zeitschr. f. Hyg. u. Infect., 54: 1-9, 1906.
71. Ueber therapeutische Verwendung von Tuberkulin. (On the therapeutic application of tuberculin.) Med. Woch., Halle, 7: 493-496, 1906.
72. Ueber die Rolle der Milch bei der Uebertragung der Tuberculose auf Menschen. (On the rôle of milk in the transmission of tuberculosis to humans.) Molkerei-Zeitz., 16: 37, 1906.
73. Ueber afrikanischen Recurrens. (African recurrent fever.) Berl. klin. Woch., 43: 185-194, 1906. Also, abstr.: Med. Bl., 29: 118, 1906. Also, abstr.: Deutsche med. Woch., 32: 283, 1906. Also, transl.: Post-Graduate, New York, 21: 770-789, 1906.
74. Ueber den bisherigen Verlauf der deutschen Expedition zur Erforschung der Schlafkrankheit in Ostafrika. (On the course to date of the German Expedition for the investigation of sleeping sickness in East Africa.) Deutsche med. Woch., 32, pp. 1-8, 1906. Also: Berlin, Bernstein, 1906. 4°, 7 pp. In A.
75. Bericht über die Stätigkeit der deutschen Expedition zur Erforschung der Schlafkrankheit bis zum 25. November 1906. ((Report on the progression of the German expedition to investigate sleeping sickness to November 25, 1906.) Deutsche med. Woch., 33: 49-51; 1462; 1889-1895, 1907. Also: Berl. klin. Woch., 44: 1523-1527, 1907. Also: Berlin, Reimer, 1908. 8°, 47 pp. In C. Also, with M. Beck and F. Kleine: Arb. a. d. k. Gesundheit., 31: 1-319, 1909.
76. Im Dienst des Roten Kreuzes; Erinnerungen. (A tribute to the Red Cross; recollections.) Deutsche Rev., 1: 338-348, 1909.

77. Antrittsrede in der Akademie der Wissenschaften am 1. Juli 1909. (First address at the Academy of Science on July 1, 1909.) *Deutsche med. Woch.*, 35: 1278, 1909.
78. Zur medikamentösen Behandlung der Lungentuberkulose. (On the medical treatment of tuberculosis of the lungs.) *Therap. Rundschau*, Berl., 3: 101-103, 1909.
79. Foreword to Bandelier and Roepke's *Lehrbuch der spezifischen Diagnostik und Therapie der Tuberkulose*, —. Würzburg, 1910. In D.
80. Epidemiology of tuberculosis. *Smithsonian report for 1910*. *Zeitschr. f. Tuberk.*, 16: 115-135, 1910. Also: *Smithsonian Institution Pub.*, No. 2049, 1911.
81. *Gesammelte Werke; unter Mitwirkung von G. Gaffky und E. Pfuhl hrsgb. von J. Schwalbe.* (Collected Works; in association with G. Gaffky and E. Pfuhl, edited by J. Schwalbe. Leipzig, Thieme, 1912. 2 v. in 3. fol. In A, C, D; E, F.

BIBLIOGRAPHY OF BIOGRAPHIES

- The Koch festival. *Med. News*, 44: 687, 1884.
- Sketch by A. Johne. *Jour. Comp. Med. and Surg.*, 6: 113-128, 1885.
- Geheimrat Koch in der Deutschen Warte. *Deutsche Warte*, 1890.
- Biography by T. P. A. Stuart. *Australas. Med. Gaz.* 10: 249-255, 1890-1891.
- Bei Robert Koch. By P. Lindenberg. Leipzig, 1891. 4°.
- Aus der Familienchronik von Robert Koch. By R. Viemend. *Deutsche Rev.*, 16: 87; 219, 1891.
- Koch's injections for actinomycosis. By T. Billroth. *Wien. klin. Woch.*, 10, 1891.
- Biography by W. Becker. Berlin, 1891, 3 Aufl., 8°.
- Biography. *Prov. Med. Jour.*, Leicester, 10: 1, 1891.
- Koch's contributions to tuberculin. By F. Hueppe. *Berl. klin. Woch.*, 28: 1121-1122, 1891.
- Koch's visit to South Africa. *South African Med. Jour.*, 4: 211-214, 1896-1897.

Biography. *Méd. Mod.*, Paris, 7: suppl., 169, 1896.

Sketch. *Brit. Med. Jour.*, 1: 1547, 1897.

Festschrift. Jena, 1903. 2°.

Sketch by L. von Schrötter. *Deutsche med. Press*, 7: 172-180, 1903.

Sketch by R. Paltz. *Wien. klin. Woch.*, 16: 1377-1381, 1903.

A dinner to Dr. Robert Koch. *New York Med. Jour.*, 86: 742-749, 1903.

Empfangsfest von Robert Koch in Tokyo, June 16, 1903. Tokyo, 1903, 2°.

Sketch in München *med. Woch.*, 55: 2253, 1903.

Koch, an appreciation. By G. A. Knopf. *Brit. Jour. Tuberculosis*, 1909, 3: 735-738, 1909.

Biography by A. Netter. *Mém. Soc. de biol.*, Paris, 69: 19-24, 1910.

Biography by C. Fraenkel. *München. med. Woch.*, 57: 1349, 1910.

Biography by F. G. Gade. *Norsk. Mag. f. Lægevidensk.*, 5. r., 2: 762-774, 1910.

Biography by H. Roger. *Presse méd.*, 12 *journees*: 449-451, 1910.

Biography by C. J. M. *Proc. Roy. Soc. Lond.*, 83: suppl. pp. xviii-xxiv, 1910-1911.

Sketch by B. Gosio. *Policlin. Roma*, 17: sez. med., 285-305, 1910.

Dr. Koch, the father of preventive medicine. By J. B. Huber. *Scient. Am.*, New York, 102: 423; 490, 1910.

Biography by F. Mesnil. *Rev. gén. d. sc. pures et appliq.*, 21: 537, 1910.

Biography by P. Ehrlich. *Rev. internat. de la tuberc.*, 17: 443-449, 1910.

Biography by P. Nobecourt. *Rev. de la tuberculose*, 2. s., 7: i-iii, 1910.

Biography by P. Aaser. *Tidsskr. f. d. norske Lægefor.*, 30: 552-555, 1910.

Biography by S. Belfanti. *Tuberculosi*, Milano, 3: 1-14, 1910-1911.

- Biography by V. Ellermann. *Ugesk. f. Laeger*, 72: 644-648, 1910.
- Biography by M. Kirchner. *Zeits. f. Tuberk.*, 16: 105-114, 1910.
- Biography by A. Netter. *Compt. rend. Soc. de biol., Paris*, 59: 1-6, 1910.
- Biography by Meinicke. *Deutsche Aerzte-Zeitg.*, 39: 265-267, 1910.
- Necrology. By B. Mollers. *Ibid.*, 39: 473-478, 1910.
- Biography by G. Gaffky. *Deutsche med. Woch.*, 36: 2321-2324, 1910.
- Biography by J. Bordet. *Jour. méd. de Brux.*, 15: 373-377, 1910.
- Biography by G. S. Woodhead. *Jour. Path. and Bacteriol., Cambridge*, 15: 108-114, 1910-1911.
- Biography. *Lancet*, London, 1: 1583-1588, 1910.
- Krankheitsgeschichte Robert Koch's. By L. Brieger and F. Kraus. *Deutsche med. Woch.*, 36: 1045, 1910.
- Der Anteil Kochs an der Malaria-forschung. By R. Ruge. *Malaria. Internat. Arch.*, 2: 168-170, 1910.
- Obituary. *Brit. Med. Jour.*, 1: 1384-1389, 1910.
- Biography by P. Ehrlich. *Chicago Med. Recorder*, 32: 443-450, 1910.
- Biography by R. Pfeiffer. *Berl. klin. Woch.*, 47: 1045-1048, 1910.
- Sketch by S. A. Knopf. *Tuberculosis*, 1910.
- Robert Koch and his achievements. Editorial. *Jour. Amer. Med. Assn.*, 54: 1772-1876, 1910.
- Sketch by E. Pfuhl. *Deutsche med. Woch.*, 37: 1399; 1443; 1483; 1524, 1911; 3: 182-199, 1911; Also: *Deutsche Rev.*, 38: 1101; 1148; 1195, 1912.
- The life and work of Koch. By W. W. Ford. *Johns Hopkins Hosp. Bull.*, 22: 415-425, 1911.
- Koch, the father of the modern science of tuberculosis. By S. A. Knopf. *Ibid.*, 22: 425-428, 1911.
- Memorial address by J. A. Wyeth. *Med. Rec.*, 79: 95-97, 1911. Also: *Amer. Jour. Obst.*, 63: 482-484, 1911.

- The discovery of the tubercle bacillus. By A. T. Laird. Alb. Med. Ann., 32: 311-318, 1911.
- Gedächtnisrede auf Robert Koch. By G. Gaffky. Tuberculosis, Berlin, 10: 1-12, 1911.
- Biography by K. Wezel. Berlin, Hirschwald, 1912. 8° roy. 156 pp.
- Robert Koch's Entwicklung zum bahnbrechenden Forscher. By Pfuhl. Deutsche Rev., 2: 338-356, 1912.
- Robert Koch zum Gedächtnis. By J. Schwalbe. Deutsche med. Woch., 39: 157; 2441; 2468, 1913.
- Erinnerungen aus der Zeit der ätiologischen Tuberkuloseforschung: Robert Koch. By P. Ehrlich. Ibid., 39: 2444-2446, 1913.
- Robert Koch und das Spezifitätsproblem. By W. Kolle. Ibid., 39: 2446-2448, 1913.
- Zur Erinnerung an Robert Koch. By W. Kolle. Med. Klin., 9: 2137; 2159, 1913.
- A monument to Koch in Japan. Editorial. Jour. Amer. Med. Assn., 62: 213, 1914.
- Dem Andenken Robert Koch. By G. Gaffky. Deutsche med. Woch., 42: 653-655, 1916.
- Sketch by F. Neufeld. Zeits. f. ärztl. Fortbild., 13: 349, 1916.
- Sketch. Jour. Amer. Med. Assn., 67: 1953, 1916.
- Enthüllung des Robert Koch—Denkmals. Deutsche med. Woch., 42: 704, 1916.
- Biography by H. C. Ernst. Proc. Amer. Acad. Arts and Sc., 53: 825-827, 1918.
- Essays on tuberculosis. III. Robert Koch. By A. K. Krause. Jour. Outdoor Life, 15: 97-101; 101-109; 120, 1918.
- Medical reminiscences; a call upon Robert Koch in his laboratory in 1902. By E. R. Baldwin. Jour. Outdoor Life, 16: 302, 1919.
- Biography. Med. Life, 29: 207, 1922; 31: 352-370, 1924; 39: 164, 1932.
- Biography. Med. Jour. Australia, 1: 413, 1923.
- Biography. Hygeia, 2: 97, 1923; 5: 59, 1927; 6: 222, 1928.
- Biography. Crusader, 14: 18, 1923.

- Diary. Biography by F. Kleine. *Deutsche med. Woch.*, 50: 21-24; 55; 88; 121; 152; 184; 216; 248, 1924.
- Biography by V. Robinson. *Med. Life*, New York, 31: 336-374, 1924.
- Biography by M. Kirchner, Vienna, 1924.
- Biographical notes bearing on Koch, Ehrlich Behring and Löffler, with portraits and letters from three of them. By G. H. F. Nuttall. *Parasitology*, 16: 214-238, 1924-1925.
- Koch, the death fighter. By P. de Kruif. In *Microbe Hunters*, New York, Harcourt, Brace and Co., 1926. Ch. 5, pp. 105-144.
- Biography by I. Goldston. *Med. Life*, 33: 589-591, 1926.
- Fiftieth anniversary of his first work. By A. Walter. *Ref. de med.*, Rosario, 2: 41-44, 1927.
- Letters. (Briefe aus vergangenen Tagen.) *Deutsche med. Woch.*, 55: 1772, 1929.
- Biography by E. E. Meyer. Valencia, Mora, 1929. 24 pp. 25.5 cm. Also, repr.: *Revista Lig. tuber.*, pp. 255-256, July-August, 1929.
- Medizin und Philosophie*. München. *med. Woch.*, 76: 10-13, 1929.
- Twentieth anniversary of death. By M. Hahn. *Med. Klin.* 26: 796, 1930.
- Biography by M. Miyajima. Geneva, "Sonor", 1931. 99 pp. port., 17.5 cm.
- Biography. *New England Jour. Med.*, 204: 942-944, 1931.
- Biography by J. Alvarez Sierra. *Día. méd.*, 3: 587, 1931.
- High lights in the life of Robert Koch. By H. Subin. *Jour. Med. Soc. New Jersey*, 28: 342-343, 1931.
- Memorial volume in honor of fiftieth anniversary of discovery of tubercle bacillus. *Med. Klin.*, 28: 387-424, 1932.
- Effect of discovery of tubercle bacillus on hygiene. By P. Uhlenhuth. *Ibid.*, 387-393, 1932.
- Effect of discovery of tubercle bacillus on pathologic anatomy of tuberculosis. By L. Aschoff. *Ibid.*, 394-395, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By T. Brugsch. *Ibid.*, 395-398, 1932.

- Effect of discovery of tubercle bacillus on pediatrics. By H. Kleinschmidt. *Ibid.*, 398-400, 1932.
- Effect of discovery of tubercle bacillus on gynecology. By M. Henkel. *Ibid.*, 400-401, 1932.
- Effect of discovery of tubercle bacillus on surgery and on surgical tuberculosis. By O. Stahl. *Ibid.*, 402-403, 1932.
- Influence of discovery of tubercle bacillus on otorhinolaryngology. By A. Brüggemann. *Ibid.*, 404-405, 1932.
- Discovery of tubercle bacillus in relation to dermatology. By J. Jadassohn. *Ibid.*, 406-407, 1932.
- Announcement of discovery of tubercle bacillus before Congress on Internal Medicine in Wiesbaden, in 1882. *Ibid.*, 420-423, 1932.
- Memorial volume in honor of fiftieth anniversary of discovery of tubercle bacillus. *Med. Welt*, 6: 325-364, 1932.
- In memory of March 24, 1882, day on which Robert Koch announced his discovery of tubercle bacillus. By R. Pfeiffer. *Ibid.*, 325-327, 1932.
- In memory of fiftieth anniversary of day on which Robert Koch announced his discovery of tubercle bacillus. By W. Kolle. *Ibid.*, 328-332, 1932.
- Fifty years since discovery of tubercle bacillus. By R. Otto. *Ibid.*, 333-334, 1932.
- Koch and development of communal hygiene. By Von Drigalski. *Ibid.*, 348-350, 1932.
- Work in federal health department. By L. Haendel. *Ibid.*, 351-353, 1932.
- Koch and laws for prevention of communicable diseases. By O. Lentz. *Ibid.*, 354-356, 1932.
- Expeditions for study of relapsing fever in 1905 and trypanosomiasis in 1906. By R. Kudicke. *Ibid.*, 359-362, 1932.
- Personal reminiscences. By C. Benda. *Ibid.*, 362-363, 1932.
- Life and work. By J. Martens. *Ibid.*, 363-364, 1932.
- Memorial volume in honor of fiftieth anniversary of discovery of tubercle bacillus. *Zeits. f. Tuberk.* 64: 1-126, 1932.
- Influence of discovery of tubercle bacillus on clinical knowledge of tuberculosis. By A. Goldscheider. *Ibid.*, 476-478, 1932.

- Effect of discovery on pathologic morphology and general pathology of tuberculosis. By Lubarsch. Ibid., 478-481, 1932.
- Influence of Koch's discovery and teachings on surgery. By E. Payr. Ibid., 481-487, 1932.
- Life work in its effect on public welfare. By C. Hamel. Ibid., 487-488, 1932.
- Influence on Prussian Board of Health. By Schopohl. Ibid., 489-490, 1932.
- Effect of discovery on knowledge of immunity. By R. Pfeiffer. Ibid., 490-493, 1932.
- Importance of discovery of tubercle bacillus in therapy and prophylaxis of infectious diseases. By W. Kolle. Ibid., 493-495, 1932.
- Koch's discovery in relation to clinical aspects of infectious diseases. By U. Friedemann. Ibid., 495-497, 1932.
- Work in field of tuberculosis. By F. Neufeld. Ibid., 497-499, 1932.
- Clinical significance of discovery of tubercle bacillus. By E. von Romberg. Ibid., 64: 3-6, 1932.
- Robert Koch. By F. Sauerbruch. Ibid., 7-9, 1932.
- Results of discovery of tubercle bacillus. By R. Philip. Ibid., 9-16, 1932.
- Significance of discovery of tubercle bacillus for pathologic anatomy. By P. Huebschmann. Ibid., 17-23, 1932.
- Work in relation to modern experimental research on tuberculosis. By B. Lange. Ibid., 31-38, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By A. Calmette. Ibid., 239-245, 1932. Also: Bull. Acad. de méd., Paris, 107: 346-355, 1932. Also: Presse méd., 40: 387-389, 1932.
- Robert Koch and combat of tuberculosis; fiftieth anniversary of discovery of tubercle bacillus. By F. A. Weber. Ztschr. f. Tuberk., 64: 399-415, 1932.
- Robert Koch-Ehrung. Deutsche med. Woch., 58: 423 only, 1932.
- Memorial volume in honor of fiftieth anniversary of discovery of tubercle bacillus. Ibid., 475-518, 1932.

- Contribution to experimental research on tropical diseases. By F. K. Kleine. *Ibid.*, 505-508, 1932.
- Robert Koch and England. By W. Bulloch. *Ibid.*, 508-509, 1932.
- Robert Koch and Japan. By M. Miyajima. *Ibid.*, 509-510, 1932.
- Fiftieth anniversary of discovery of causative agent of tuberculosis. By R. Pfeiffer. *Forsch. u. Fortschr.*, 8: 113-115, 1932.
- Problem of tuberculosis in 1882 and in 1932; account of fiftieth anniversary of discovery of tubercle bacillus; historical note. By S. Sterling. *Polska gaz. lek.*, 11: 213-217, 1932.
- Significance of discovery of tubercle bacillus. By E. Zimmermann. *Zeits. f. Med.-Beamte*, 45: 93-107, 1932.
- Koch and tuberculin therapy. By W. Neumann. *Wien. med. Woch.*, 82: 407-408, 1932.
- Work in hygiene. By E. Glaser. *Ibid.*, 435-438, 1932.
- What Koch meant to tuberculosis. By L. Brown. *Libman Anniv. Vols.*, 1: 253-264, 1932.
- Work of Koch as basis for recent developments in clinical study of tuberculosis. By M. R. Borok. *Sovet. vrach. gaz.*, pp. 901-906, 1932.
- Koch and his conception of problem of tuberculosis. By E. E. Ben and M. L. Goldfarb. *Ibid.*, pp. 1248-1252.
- Biography by Gnant. *Med. Kor.-Bl. f. Württemberg*, 102: 192-196, 1932.
- Life work: in memory of fiftieth anniversary of discovery of tubercle bacillus. By R. Hilgermann. *Zeits. f. Gesundh.*, 24: 105-108, 1932. Also: *Prakt. Desinf.*, 24: 131-136, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. *Zeits. f. Hyg. u. Infekt.*, 113, Hft. 4, 1932.
- Reminiscences of African expedition. By F. K. Kleine. *Fortschr. d. Med.*, 50: 959-966, 1932.
- Discovery of etiology of tuberculosis. By O. Roepke. *Zeits. f. Bahnärzte*, 27: 59-69, 1932.
- Biography by W. Kolle. *Zentralbl. f. Bakt.*, 127: 3-10, 1932.
- Speech on fiftieth anniversary of discovery of tubercle bacillus. By R. Maresch. *Wien. klin. Woch.*, 45: 417-419, 1932.

- Address delivered at fiftieth anniversary of discovery of tubercle bacillus. By N. Jagić. *Ibid.*, 419-421, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By F. Hamburger. *Ibid.*, 421-422, 1932.
- Value of discovery of tubercle bacillus to medical science. By J. L. A. Peutz. *Geneesk. gids.*, 10: 295-303, 1932.
- Discovery of tubercle bacillus. By A. de Besche. *Nord. med. tidskr.*, 4: 193-195, 1932.
- Biography by G. Schröder. *Tuberkulose*, 12: 45-47, 1932.
- Biography by Bruno Heymann. Leipzig, 1932. 353 pp.
- Discovery of tubercle bacillus. By D. Okolicsányi-Kuthy. *Budapesti orvosi ujság.*, 30: 481-483, 1932.
- The rôle of Robert Koch in combating tuberculosis. By J. Geszti. *Ibid.*, 553-558, 1932.
- Announcement of discovery of tubercle bacillus. By H. Unger. *Zeits. f. ärztl. Fortbild.*, 29: 189-191, 1932.
- In memoriam. By F. A. Weber. *Ibid.*, 404-409, 1932.
- Discovery of tubercle bacillus. By O. von Hellens. *Finska läk.-sällsk. handl.*, 74: 125-127, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By A. Ferrannini. *Riforma med.*, 48: 413-415, 1932.
- Work of Italian Clinical schools in application of Koch's discovery of tubercle bacillus. By N. Pende. *Ibid.*, 1901-1902, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By A. Filippini. *Policlinico (sez. prat.)* 39: 581-582, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By R. Hernández del Castillo. *Med. ibera*, 1: cxlix-cli, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By B. Heymann. *Klin. Woch.*, 11: 489-490, 1932.
- Biography by Z. Szymanowski. *Warszawskie czasop. lek.*, 9: 271-273, 1932.
- Personal memories. By O. Bujwid. *Ibid.*, 9: 273-275, 1932.
- Discovery of tuberculin. By Z. Srebrny. *Ibid.*, 275-278, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By K. Kisskalt. *München. med. Woch.*, 79: 497-501, 1932.
- Description of Koch celebration in Berlin, March 5, 1932. *Veröffentl. a. d. Geg. d. Med.-Verwalt.*, 37: 1-50, 1932.

- Discovery of anthrax spores and tubercle bacilli. By G. Venzmer. *Mikrokosmos*, 26: 5; 29, 1932.
- In memory of the great scientist and his importance in medicine. By W. Kolle. *Arb. a. d. Staatsinst. f. exper. Therap.*, Hft. 26, pp. 1-10, 1932.
- Active campaign against tuberculosis in Russia in connection with observance of Koch jubilee. By S. E. Nezlin. *Bor. s. tuberk.*, 10: 525-527, 1932.
- Life and significance of Robert Koch in microbiology and epidemiology. By V. A. Lyubarskiy. *Bor. s. tuberk.*, 10: 537-544, 1932.
- Evolution of study of tubercle bacillus from time of Koch to present day. By O. I. Bronshteyn. *Ibid.*, 544-553, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By L. Pekanovich. *Orvosi hetil.*, 76: 263, 1932.
- Discovery of tubercle bacillus by Robert Koch. *Tijdschr. v. sociale hyg.*, 34: 138-140, 1932.
- Contributions of Koch to knowledge of tuberculosis. By A. Ilvento. *Lotta contro la tuberc.*, 3: 828-832, 1932.
- Present status of clinical concept of pulmonary tuberculosis at fiftieth anniversary of discovery of tubercle bacillus, with biographical sketch of Koch. By R. Royo Villanova. *Clín. y lab.*, 21: 365-386, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By F. K. Kleine. *Rev. méd. german.-ibero-am.*, 5: 113-115, 1932.
- Life. By P. Farreras. *Rev. espan. de med. y cir.*, 15: 119-121, 1932.
- Robert Koch and his discoveries in tuberculosis. By A. Cerveró Lacort. *Mundo méd.*, 14: 760-768, 1932.
- In memoriam. By A. Raimondi. *Rev. Asoc. méd. argent.*, 46: 419-421, 1932.
- In memoriam. By A. Bachmann. *Ibid.*, 421-428, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By F. Buonomo La Rossa. *Rassegna internaz. di clin. e terap.*, 13: 328-329, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By S. Coelho. *Med. contemp.*, 50: 169-173, 1932.

- Fiftieth anniversary of discovery of tubercle bacillus. By J. Torres Gost. *Rev. españ. de tuberc.*, 3: 209-221, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus: biographical sketch of Koch. By A. Pruneda. *Gac. méd. de México*, 63: 268-273, 1932. Also: *Rev. méd. german.-ibero-am.*, 5: 497-501, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By F. deP. Miranda. *Salubridad*, 3: 225-227, 1932.
- En memoria—por Codina Castellvi, José. *Anales Acad. nac. med.* 1932, 2 época, tomo 4, cuaderno 2, 2 trimestre, p. 251-268, 1932.
- Discovery of tubercle bacillus. By L. Bernard. *Rev. de la tuberc.*, 13: 506-509, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus; thoughts in honor of Koch's genius. By Martin Salazar. *Rev. san. mil.*, Madrid, 22: 97-99, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By M. Lelong. *Paris méd. (annexe)*, 1: x-xi, 1932.
- Fiftieth anniversary of discovery of tubercle bacillus. By A. Vadone. *Prensa méd. argent.*, 18: 1377-1379, 1932.
- Discovery of tubercle bacillus on Mar. 24, 1882. By F. K. Kleine. *Tung-Chi. med. Monatschr.*, 8: 47-49, 1932.
- Discovery of tubercle bacillus by Robert Koch. By V. Puntoni. *Ann. d'ig.*, 42: 168-170, 1932.
- Influence of discovery of tubercle bacillus on medicine. By R. A. Young. *Tr. Nat. Assn. Prev. Tuberc.*, 18: 11-20, 1932.
- Influence of discovery of tubercle bacillus on preventive medicine. By W. C. White. *Ibid.*, 21-28, 1932.
- Influence of Koch's discovery on surgery, with particular reference to treatment of surgical tuberculosis. By H. Gauvain. *Ibid.*, 29-43, 1932.
- Koch anniversary, the man and his work. By D. A. Stewart. *Canad. Med. Assn. Jour.*, 26: 475-478, 1932.
- H. M. Biggs lecture. By L. Brown. *Bull. New York Acad. Med.*, 8: 558-584, 1932.
- Robert Koch and his work. By C. M. Hasselmann. *Jour. Philippine Islands Med. Assn.*, 12: 328-335, 1932.

- Robert Koch number. *Med. Life*, 39: 129-187, 1932.
- Biography by G. B. Webb. *Nat. Tuberc. Assn. Tr.*, 28: 24-38, 1932. Also: *Ann. Med. Hist.*, 4: 509-523, 1932.
- Koch's views on stability of species among bacteria. By T. Smith. *Ibid.*, 524-530, 1932.
- Reception of Koch's discovery in United States. By H. R. M. Landis. *Ibid.*, 531-537, 1932.
- Discovery of tubercle bacillus. By A. K. Krause. *Amer. Rev. Tuberc.*, 25: 285-298, 1932.
- Professor Robert Koch in Iowa in 1908. *Jour. Iowa Med. Soc.*, 22: 153-154, 1932.
- Pioneers in medicine. By C. Lillingston. *Hygeia*, 10: 248-250, 1932.
- Koch and golden anniversary of discovery of tubercle bacillus. By S. A. Knopf. *Med. Jour. and Rec.*, 135: 305-308, 1932.
- Koch and tuberculosis. By K. Emerson. *Journal-Lancet*, 52: 215-216, 1932.
- In memoriam; fiftieth birthday of tubercle bacillus. By F. Baum. *Jour. Med. Soc. New Jersey*, 29: 238-243, 1932.
- Discovery of tubercle bacillus. By S. L. Cummins. *Brit. Jour. Tuberc.*, 26: 72-75, 1932.
- Biography. *Med. Rec.*, 79: 76, 1932.
- Discovery by Koch. By L. Cobbett. *Cambridge Univ. Med. Soc. Mag.*, 9: 93-102, 1932.
- Biography by S. A. Knopf. *Unity*, Kansas City, April 11, 1932, pp. 90-91.
- Biography by H. J. Corper. *Colorado Med.*, 29: 353-362, 1932.
- Biography by Grace T. Hallock and C. E. Turner, Metropolitan Life Ins. Co. *Health Heroes*, 1932.
- What Koch meant to tuberculosis. By Lawrason Brown. In: *Contributions to Med. Sc. in Honor of D. E. Libman*, New York, International Press, 1932. Vol. 1, p. 253-264.
- Discovery of tubercle bacillus; implications and results. By R. Philip. *Brit. Med. Jour.*, 2: 1-5, 1932. Also: *Amer. Rev. Tuberc.*, 26: 637-652, 1932.

- Discovery of tubercle bacillus; importance and significance. By Y. G. Shrikhande. *Indian Med. Gaz.*, 67: 691-692, 1932.
- Discovery of the tubercle bacillus. By Helen C. Davis. *Science News Letter*, March 19, 1932.
- Discovery of cholera bacillus by Koch 50 years ago. By Frey. *Klin. Woch.*, 12: 1376-1379, 1933.
- Koch's discovery of cholera vibrio. By F. K. Kleine. *Zeits. f. arztl. Fortbild.*, 30: 385-386, 1933.
- Koch and problem of tuberculosis; fiftieth anniversary of discovery of tubercle bacillus. By M. Nasvytis. *Medicina*, Kaunas, 14: 4-13, 1933.
- The tubercle bacillus since Koch's discovery. By S. A. Petroff. *Bol. Asoc. med. de Puerto Rico*, 25: 167-175, 1933.
- Biography by E. Metchnikoff. Paris, Alcan, 1933. xi, 195 pp., 18.5 cm.
- Discovery of tubercle bacillus; implications and results. By R. Philip. *Edinburgh Med. Jour.*, 40: 146-157, 1933.
- Biographical sketch by H. E. Sigerist. In *The Great Doctors*, New York, Norton, 1933. Ch. 43, pp. 366-372.
- Biography by R. Munoz Carbonero. *Cron. med.*, Valencia, 38: 613-616, 1934.
- First criticism of Robert Koch by followers of Pettenkofer. By K. Kisskalt. *Arch. f. Hyg.*, 112: 167-180, 1934.
- Fifty years after discovery of tubercle bacillus; present status of study of tubercle bacilli and tuberculin. By H. Poindecker. *Wien, med. Woch.*, 84: 151; 178, 1934.
- Biography by A. Leber. *Geneesk. tijdschr. v. Nederl.—Indie*, 75: 1030-1034, 1935.
- Biography by P. Martell. *Zeits. f. arztl. Fortbild.*, 32: 332-335, 1935.
- Author's remembrances of Koch on twenty-fifth anniversary of his death. By B. Mollers. *Rev. med. german.—ibero—am.*, 8: 161-163, 1935.
- Unveiling of bust in Hall of Fame of German Museum in Munich. By C. Schilling. *Deutsche med. Woch.*, 61: 851, 1935.
- Koch's work. By R. Otto. *Med. Klin.*, 31: 669-671, 1935.

- Koch and landmarks in history of medicine. By D. P. Marais.
South African Med. Jour., 9: 659-663, 1935.
- American tribute. By L. Brown. Ann. Med. Hist., 7: 99-112;
292-304; 385-401, 1935.
- Biography. Amer. Jour. Surg., 27: 376, 1935.
- Koch, a singularly great doctor of medicine. By A. Beilin.
Hygeia, 13: 507, 1935.
- Biographical sketch by C. Lillingston. Ibid., March 1935.
- Note on the Koch memorial. Jour. Amer. Med. Ass., 105:
448, 1935.
- Sketch by G. B. Webb. In Tuberculosis, vol. 16 of Clio Medica.
New York, Hoeber, 1936. pp. 96-107.



Untersuchungen über Bakterien

V. Die Aetiologie der Milzbrand-Krankheit, begründet auf die Entwicklungsgeschichte des Bacillus Anthracis

VON

DR. KOCH

Kreisphysikus in Wollstein

HIERZU TAFEL XI.

Beiträge zur Biologie der Pflanzen, 2: 277-310, 1877



INLEITUNG. Seit dem Auffinden der stäbchenförmigen Körper im Blute der an Milzbrand gestorbenen Thiere hat man sich vielfach Mühe gegeben, dieselben als die Ursache für die direkte Uebertragbarkeit dieser Krankheit ebenso wie für das sporadische Auftreten derselben, also als das eigentliche Contagium des Milzbrands nachzuweisen. In neuerer Zeit hatte sich hauptsächlich Davaine mit dieser Aufgabe beschäftigt und gestützt auf zahlreiche Impfversuche mit frischem oder getrocknetem stäbchenhaltigen Blute, mit aller Entschiedenheit dahin ausgesprochen, dass die Stäbchen Bakterien seien und nur beim Vorhandensein dieser Bakterien das Milzbrandblut die Krankheit von Neuem zu erzeugen vermöge. Die ohne nachweisbare direkte Uebertragung entstandenen Milzbranderkrankungen bei Menschen und Thieren führte er auf die Verschleppung der, wie er entdeckt hatte, im getrockneten Zustande lange Zeit lebensfähig bleibenden Bakterien durch Luftströmungen, Insekten und dergl. zurück. Die Ver-

breitungsweise des Milzbrandes schien hiermit vollständig klar gelegt zu sein.

Dennoch fanden diese von Davaine aufgestellten Sätze von verschiedenen Seiten Widerspruch. Einige Forscher wollten nach Impfung mit bacterienhaltigem Blute tödlichen Milzbrand erzielt (p. 278) haben, ohne dass sich nachher Bacterien im Blute fanden, und umgekehrt liess sich wieder durch Impfung mit diesem bacterienfreien Blute Milzbrand hervorrufen, bei welchem Bacterien im Blute vorhanden waren. Andere machten darauf aufmerksam, dass der Milzbrand nicht allein von einem Contagium abhängt, welches oberhalb der Erde verbreitet werde, sondern dass diese Krankheit in einem unzweifelhaften Zusammenhange mit Bodenverhältnissen stehe. Wie würde sonst zu erklären sein, dass das endemische Vorkommen des Milzbrandes an feuchten Boden, also namentlich an Flussthäler, Sumpfdistrikte, Umgebungen von Seen gebunden ist; dass ferner die Zahl der Milzbrandfälle in nassen Jahren bedeutender ist und sich hauptsächlich auf die Monate August und September, in welchen die Curve der Bodenwärme ihren Gipfelpunkt erreicht, zusammendrängt, dass in den Milzbranddistricten, sobald die Heerden an bestimmte Weiden und Tränken geführt werden, jedesmal eine grössere Anzahl von Erkrankungen unter den Thieren eintritt.

Diese Verhältnisse sind allerdings durch die Annahme Davaine's nicht zu erklären und das Ungenügende derselben hat zur Folge gehabt, dass von Vielen die Bedeutung der Bacterien für den Milzbrand ganz geleugnet ist.

Da ich einige Male Gelegenheit hatte, Thiere, welche an Milzbrand gefallen waren, zu untersuchen, so benutzte ich diese zu einer Reihe von Versuchen, welche zur Aufklärung der eben angedeuteten dunklen Punkte in der Milzbrandätiologie beitragen sollten. Hierbei kam ich sehr bald zu der Ueberzeugung, dass die Davaine'sche Theorie über die Verbreitungsweise des Milzbrandes nur zum Theil richtig ist.

Es zeigte sich nämlich, dass die Stäbchen des Milzbrandblutes die Weitem nicht so resistent sind, als Davaine seinen Versuchen entnehmen zu müssen glaubte. Wie ich später nachweisen

werde, bewahrt das Blut, welches nur Stäbchen enthält, seine Impffähigkeit im getrockneten Zustande nur wenige Wochen und im feuchten nur einige Tage. Wie sollten also so leicht vergängliche Organismen das oft während des ganzen Winters und im feuchten Boden vielleicht Jahrelang schlummernde Contagium des Milzbrandes bilden? Hier blieb, wenn die Bacterien wirklich die Ursache des Milzbrandes abgeben, nichts anderes übrig als anzunehmen, dass die durch einen Generationswechsel in einen anderen gegen abwechselndes Eintrocknen und Anfeuchten unempfindlichen Zustand übergehen können, oder, was weit mehr Wahrscheinlichkeit hat und was von Prof. Cohn schon im zweiten Hefte, Band I. dieser Beiträge p. 145, angedeutet wurde, (p. 279) dass die Bacterien Sporen bilden, welche die Fähigkeit besitzen, nach längerem oder kürzerem Ruhezustande von Neuem zu Bacterien auszuwachsen.

Alle meine weiteren Versuche gingen nun dahin, diesen vermutheten Entwicklungszustand der Milzbrandbacterien aufzufinden. Nach manchen vergeblichen Bemühungen gelang es denn auch schliesslich dieses Ziel zu erreichen und damit die wahre Milzbrandätiologie in ihren Grundzügen festzustellen.

Da die Entwicklungsgeschichte der Milzbrandbacterien nicht nur botanisches Interesse bietet, sondern auch manches Licht auf die bis jetzt so dunkle Aetiologie der vom Boden abhängigen Infectionskrankheiten zu werfen im Stande ist, so habe ich es jetzt schon, obwohl meine Versuche noch nicht abgeschlossen sind, unternommen, die wichtigsten Resultate derselben zu veröffentlichen.

II. *Entwicklungsgeschichte des Bacillus Anthracis.* Die Milzbrandbacterien gehören nach Prof. F. Cohn's System der *Schizophyten** zur Gattung *Bacillus* und sind mit dem speciellen Namen *Bacillus Anthracis* belegt, dessen ich mich im Folgenden statt des viel umfassenden Ausdrucks Bacterien bedienen werde.

1. Im Blute und in den Gewebssäften des lebenden Thieres vermehren sich die Bacillen ausserordentlich schnell in derselben Weise, wie es bei verschiedenen andern Arten Bacterien beo-

* Band I. Heft 3 dieser Beiträge p. 202.

bachtet ist, nämlich durch Verlängerung und fortwährende Quertheilung.

Es ist mir allerdings nicht gelungen, diesen Vorgang direct zu sehen; derselbe lässt sich aber aus den schon häufig vorgenommenen und von mir in folgender Weise wiederholten Impfversuchen schliessen. Als sehr bequemes und leicht zu habendes Impfobject benutzte ich meistens Mäuse. Anfangs impfte ich dieselben an den Ohren oder in der Mitte des Schwanzes, fand aber diese Methode unsicher, da die Thiere durch Reiben und Lecken das Impfmateriel entfernen Können; später wählte ich als Impfstelle den Rücken der Schwanzwurzel, wo die Haut schon verschiebbar und mit langen Haaren bedeckt ist. Die in einem verdeckten grossen Glase sitzende Maus wird zu diesem Zwecke mit einer langen Pincette am Schwanze gefasst und letzterer aus einer schmalen Spalte zwischen Deckel und Glasrand so weit hervorgezogen, dass bequem ein flacher querverlaufender Einschnitt in die Haut des Schwanzwurzelrückens gemacht und ein möglichst kleines Tröpfchen der bacillenhaltigen Flüssigkeit (p. 280) in die kleine Wunde gebracht werden kann. In dieser Weise ausgeführte Impfungen, welche ich in grosser Zahl gemacht habe, hatten ausnahmslos ein positives Resultat, sobald ganz frische Milzbrand-Substanzen angewandt wurden; und ich glaube deswegen eine derartige Impfung, je nach ihrem Erfolg, als ein sicheres Reagens auf das Leben oder Abgestorbensein der Bacillen ansehen zu Können: eine Ansicht, welche durch andere, später zu erwähnende Versuche als richtig erwiesen wird.

Theils nun, um immer mit frischem Material versehen zu sein, theils aber auch um zu prüfen, ob nicht nach einer bestimmten Zahl von Generationen die Bacillen in eine andere Form übergehen, wurden mehrere Male Mäuse in aufeinanderfolgender Reihe geimpft, so dass ohne Unterbrechung die folgende Maus immer mit der Milzsubstanz der kurz vorher an Milzbrand gestorbenen inficirt wurde. Die längste dieser Reihen betrug zwanzig Mäuse, so dass also eben so viele Bacillengenerationen vorlagen; aber bei sämmtlichen Thieren ergab sich derselbe Befund; immer war die Milz erheblich geschwollen und mit zahllosen Mengen von glashellen Stäbchen gefüllt, welche geringe Grössendifferenzen hatten, unbeweglich waren und keine Sporenbildung

oder dergleichen zeigten. Dieselben Bacillen fanden sich auch, aber bei weitem nicht so zahlreich als in der Milz, im Blute. Bei diesem Versuche hatten sich also durch viele Generationen aus wenigen Bacillen immer wieder bedeutende Massen ebenso gestalteter Individuen derselben Art entwickelt und da man unter diesen neu entstandenen Bacillen viele mit einer beginnenden Quertheilung in ihrer Mitte, manche an dieser Stelle geknickte und noch andere unter einem Winkel lose zusammenhängende erblickt, so lässt sich wohl eine andere Weise ihrer Vermehrung als durch Verlängerung und Quertheilung, nachdem sie ungehähr die doppelte Länge erreicht haben, kaum annehmen. Es dürfte aber auch nach diesem Resultat schwerlich zu erwarten sein, dass durch noch längere Reihen von Impfungen eine Formveränderung der Bacillen erreicht werden, oder dass man schliesslich auf einen Generationswechsel derselben treffen könnte. Auch in dem der Impfstelle benachbarten serös infiltrirten Unterhautzellgewebe und in den nächsten Lymphdrüsen fand ich bei Kaninchen und Meerschweinchen nur kurze und in der Theilung begriffene Stäbchen.

Die Vertheilung der Bacillen im Körper der geimpften Thiere ist nicht immer gleichmässig. Bei Meerschweinchen enthielt das Blut ausserordentlich viele Bacillen, so dass ihre Zahl oft derjenigen der rothen Blutkörper gleichkam oder sie selbst übertraf; im Blute (p. 281) der Kaninchen sind sie erheblich weniger zahlreich, oft so selten, dass man mehrere Gesichtsfelder durchmustern muss, ehe man einige findet; bei Mäusen enthält das Blut stets eine so geringe Zahl Bacillen, dass sie manchmal zu fehlen scheinen.* Dafür findet man bei Kaninchen die Bacillen um so reichlicher und sicherer in den Lymphdrüsen und in der Milz, und bei Mäusen in erstaunlicher Menge in der Milz. Einigemale habe ich die Marksubstanz der Tibia von Mäusen untersucht, aber nur vereinzelte Bacillen darin gefunden.

Auf weitere hierher gehörige Details über die Lagerung der Bacillen im Gewebe der Milz, in den Blutgefässen, über ihre

* Derartige Fälle haben wahrscheinlich, wenn nur das Blut der mit Milzbrand geimpften Thiere untersucht wurde, zur früher erwähnten Ansicht geführt, dass Milzbrand, ohne dass Bacillen im Blute sich finden, vorkomme und dass man durch Impfung mit bacillenfreiem Blute wieder Milzbrand erzeugen könne.

Anhäufungen in den Capillaren und kleinen Venen und die dadurch bedingten lokalen Oedeme, Gefässzerreissungen und Blutaustritte vermag ich wegen des rein pathologischen Interesses dieser Verhältnisse hier nicht weiter einzugehen.

Ebenso würde es zu weit führen, die Frage nach der eigentlichen Todesursache der an Milzbrand sterbenden Thiere zu erörtern, ob dieselben durch die bei dem intensiven Wachsthum der Bacillen im Blute entwickelte Kohlensäure oder, was wohl wahrscheinlicher ist, durch giftig wirkende Spaltprodukte der von den Parasiten zu ihrer Ernährung verbrauchten Eiweisskörper getödtet werden.

2. Im Blute des todten Thieres odern in geeigneten andern Nährflüssigkeiten wachsen die bacillen innerhalb gewisser Temperaturgrenzen und bei Luftzutritt zu ausserordentlich langen, unverzweigten *Leptothrix*-ähnlichen Fäden aus, unter Bildung zahlreicher Sporen.

Am einfachsten überzeugt man sich von der Richtigkeit dieses Satzes durch folgendes Experiment:

Auf den Objectträger wird ein Tropfen von möglichst frischem Rinderblutserum oder *Humor aqueus* von Rinderaugen gebracht, in diesen ein kleines Stückchen frische bacillenhaltige Milzsubstanz eingetragen und das Deckgläschen so darauf gelegt, dass die Bacillenmasse ungefähr in die Mitte des Präparats zu liegen kommt. Hierauf wird der Objectträger, um die Verdunstung der Flüssigkeit zu verhüten, sofort in einen feuchten Raum gebracht und mit diesem in den Brütkasten gestellt.*

* Als feuchten Raum benutzte ich flache mit nassem Sand gefüllte Teller; auf dem Sand lag eine Schicht Filtrirpapier und auf diesem die Präparate. Der Teller wurde mit einer Glasplatte bedeckt. Wenn die Sandschicht so hoch ist, dass der Abstand zwischen der Oberfläche der Präparate und der unteren Seite der Glasplatte $\frac{1}{2}$ bis 1 Ctm. beträgt, dann bleiben die Präparate genügend feucht. Der von mir angewandte Brütapparat, welcher sechs auf einander gestellte Teller mit Präparaten aufnehmen konnte, wurde in Ermangelung von Gas durch eine mit Cylinder versehene Petroleumlampe erwärmt. Allen, welche ohne Gas oder ohne Regulator derartige Versuche mit dem Brütapparat unternehmen wollen, kann ich diese Methode der Heizung nicht genug empfehlen. Da man mit einer kleinen Flamme einen grossen Apparat genügend erwärmen kann, so ist bei einem einigermaßen grossen Petroleumreservoir der Lampe nur nöthig, dieselbe ungefähr täglich einmal zu füllen und die Höhe der Flamme für die gewünschte Temperatur richtig auszuprobiren, um ohne besondere Mühe oder Aufsicht fortwährend eine kaum um 1-2° schwankende Temperatur zu haben.

(p. 282) Der Wassergehalt der Luft in dem feuchten Raum muss so reguliert werden, dass die Flüssigkeit nicht unter dem Deckglase hervordringt und dass das Serum am Rande des Deckglases nicht eintrocknet. Im ersteren Falle werden die Bacillen unter dem Deckgläschen weggeschwemmt und entgehen der Beobachtung, im letzteren wird durch die trockne Randschicht des Serums die Luft von den Bacillen abgesperrt und jede weitere Entwicklung derselben damit verhindert.

Die so zubereiteten Präparate bleiben 15–20 Stunden im Brütapparat bei einer Temperatur von 35–37°. Bei einer alsdann vorgenommenen Untersuchung finden sich in der Mitte des Präparats (Taf. XI. Fig. 1) zwischen den noch gut erhaltenen Zellen der Milzpulpa und den Blutkörperchen (a, b) noch viele unveränderte Bacillen, jedoch in geringerer Zahl als im frischem Präparate. Sobald man aber die Mitte des Präparates verlässt, trifft man auf Bacillen, welche um das 3–8 fache verlängert sind und dabei einige leichte Knickungen und Krümmungen zeigen (Fig. 2). Je näher man nun dem Rande des Deckglases kommt, um so längere Fäden findet man, welche vielfach gewunden sind und schliesslich die hundert- und mehrfache Länge der ursprünglichen Bacillen erreichen (Fig. 3). Viele dieser langen Fäden haben ihre gleichmässige Struktur und ihr glashelles Aussehen verloren, ihr Inhalt ist fein granuliert und stellenweis treten in demselben kleine stärker lichtbrechende Körnchen in regelmässigen Abständen auf (Fig. 3a). In den dicht am Rande befindlichen Fäden, welche also in Bezug auf den Gasaustausch in der Nährflüssigkeit am günstigsten liegen, ist die Entwicklung am weitesten vorgeschritten; sie enthalten vollständig ausgebildete Sporen, welche in der Gestalt von etwas länglich runden, (p. 283) stark lichtbrechenden Körpern in ganz regelmässigen kurzen Abständen der Substanz der Fäden eingelagert sind (Fig. 4a). In dieser Form gewähren die Fäden, namentlich wenn sie in vielfach verschlungenen und um einander gewundenen Linien gruppiert sind, einen überraschenden Anblick, der sich am besten mit demjenigen höchst zierlicher, künstlich angeordneter Perlschnüre vergleichen lässt.

Manche Fäden sind auch schon in der Auflösung begriffen und

ihre frühere Gestalt nur noch durch die reihenförmige Lagerung der von einer schleimigen Bindesubstanz zusammen gehaltenen Sporen angedeutet. Dazwischen liegen dann bisweilen einzelne freie und kleine Häufchen zusammen geballter Sporen (Fig. 4b). In einem einzigen solchen gut gelungenen Präparate sind also alle Uebergänge von dem kurzen Bacillusstäbchen bis zu langen sporenhaltigen Fäden und freien Sporen vertreten und es könnte damit schon der Beweis dafür gebracht sein, dass letztere aus ersteren hervorgegangen sind. Trotzdem ich anfangs diesen Versuch mehrfach wiederholte und immer wieder zu demselben Resultate kam, stiegen mir doch verschiedene Bedenken gegen die Richtigkeit dieser Annahme auf. Wie kamen die Bacillen, an denen ich bis dahin keine selbständige Bewegung wahrgenommen hatte, an den Rand des Präparates, während die Blutkörperchen in der Mitte liegen blieben? Konnten die langen sporenhaltigen Fäden nicht möglicherweise am Rande der Flüssigkeit durch aus der Luft dahin gelangte Keime entstanden sein? Denn gegen eine derartige Verunreinigung aus der Luft waren die Präparate nicht geschützt und in der That wucherten neben den Fäden auf diesem Wege oft die schönsten Colonien von *Micrococcus* und *Bacterium* in das Präparat hinein; einigemal erschien auch eine der unsrigen ähnliche Bacillusart. Hier kam also Alles darauf an, vollständige Sicherheit zu erlangen und nicht in einen Fehler zu verfallen, welcher leider schon so oft bei Culturversuchen mit den niedersten Organismen von erfahrenen Forschern begangen ist und durch welchen die Untersuchungen auf diesem Gebiete in neuerer Zeit etwas in Misscredit gekommen sind. Ich meine den Fehler, ähnliche Formen, welche in derselben Nährflüssigkeit zu gleicher Zeit oder kurz nacheinander entstanden und zugleich mit scheinbaren Uebergangsformen vermischt sind, ohne Weiteres als verschiedene Entwicklungsstadien desselben Organismus zu erklären.

Da mir die Bedingungen für die Entwicklung des *Bacillus Anthracis* bekannt waren, nämlich die Nährflüssigkeit, die Temperatur bei welcher er wächst und die Nothwendigkeit der Luftzufuhr, so versuchte ich auf dem Mikroskoptisch diese Erfordernisse (p. 284) herzustellen, um so direkt die Veränderung der Bacillen beobachten zu können.

So schwierig ich mir anfangs die Ausführung dieses Versuches vorgestellt hatte, so einfach gestaltete er sich in der Wirklichkeit. Nach manchem missglücktem Experiment fand ich folgende Methode als die Zweckmässigste:

Als Wärmequelle diente ein M. Schulze'scher heizbarer Objectisch, welchen ich, ebenso wie früher vom Brütapparat angegeben ist, mit einer Petroleumlampe erwärmte. Das Mikroskop muss allerdings auf einen Untersatz gestellt werden, um die Lampe, welche mit einem flachen, aus Blech gearbeiteten Petroleumreservoir versehen ist, mit ihrem Cylinder unter den Arm des heizbaren Objectisches zu bringen. Eine einzige kleine Flamme, ungefähr unter der Mitte des einen Arms stehend, genügte bei meinem Apparat, umtagelang den Objectisch auf der erforderlichen Temperatur zu erhalten. Der feuchte, lufthaltige Raum wurde von einem durch das Deckglas geschlossenen hohlgeschliffenen Objectträger ersetzt (Fig. 6). Das den Bacillen hierdurch für ihre Entwicklung gewährte Luftquantum ist sehr gering, aber wie die Erfahrung lehrt, genügt es zum Gelingen des Versuches. Um nun die richtige Temperatur für die von mir angewandte Sorte von hohlgeschliffenen Objectträgern zu finden, benutzte ich den Schmelzpunkt von Rindertalg, welcher im Wasserbade auf ziemlich genau 40° bestimmt war. Von diesem vorher geprüften Rindertalg wurde ein Tröpfchen auf ein Deckglas gebracht und dieses durch eine rings um die Höhlung des Objectträgers gepinselte Schicht Provenceröl luftdicht, und zwar mit dem Talgtröpfchen nach unten gerichtet, auf den Hohlraum des Objectträgers aufgesetzt. Es ergab sich dabei, dass der Objectisch auf 45° erwärmt werden musste, um den Tropfen unter dem Deckglase eben zum Schmelzen zu bringen. Für die zu meinen Versuchen erforderliche Temperatur genügte es also, den Objectisch so zu heizen, dass sein Thermometer dauernd auf 40° zeigte. Zu gleicher Zeit musste es auffallen, dass eine Annäherung des Tubus, wie sie zur Einstellung eines Objectes für Hartnack Obj. 7 Ocul. 3, welche ich bei diesen Untersuchungen benutzte, erforderlich ist, jedesmal stark abkühlend wirkte und die Temperatur in dem Tropfen um 5 bis 8° herabsetzte. Nach diesen Ermittlungen brachte ich auf die untere Seite des Deckglases einen Tropfen frisches Rinderblutserum oder, was sich für

diesen Versuch noch viel besser bewährte, einen Tropfen ganz frischen und möglichst reinen *Humor aqueus* von Rinderaugen. Der Tropfen darf natürlich nur so dick sein, dass (p. 285) man noch alle seine Schichten mit dem Mikroskop durchmustern kann.* Hierauf wurde in den Rand des Tropfens eine möglichst geringe Menge ganz frischer bacillenhaltiger Milzsubstanz eingetragen und das Deckgläschen sofort auf den mit Oel bestrichenen Objectträger gelegt. Der kleine Hohlraum füllt sich schnell mit Wasserdampf und die anfängliche Verdunstung des Tropfens ist so gering, dass nur am äussersten Rand einige Bacillen vertrocknen; später behält der Tropfen tagelang unverändert seine Gestalt. Das so hergerichtete Präparat wurde nun auf den geheizten Objecttisch gebracht und nachdem die Strömungen in der sich erwärmenden Flüssigkeit sich gelegt hatten, einige mehr nach dem Innern des Tropfens zu gelegene Bacillen fixirt, rasch noch ihre Form und Lage gezeichnet und dann der Tubus hinaufgeschoben, um eine ungleichmässige und zu lange Abkühlung des Präparates zu vermeiden. Bei der nun folgenden alle 10 bis 20 Minuten vorgenommenen Untersuchung wurde wahrgenommen, dass die Bacillen anfangs etwas dicker werden und anscheinend aufquellen, sich aber in den ersten beiden Stunden kaum merklich ändern. Dann aber beginnt ihr Wachstum. Schon nach 3 bis 4 Stunden haben sie die 10–20 fache Länge erreicht, sie fangen sich an zu krümmen, gegenseitig zu verdrängen oder geflechtartig durcheinander zu schieben. Nach einigen weiteren Stunden sind die einzelnen Fäden schon so lang,

* Unter verschiedenen Arten hohlgeschliffener Objectträger fand ich am bequemsten einen von 3 Mm. Dicke, welcher, beiläufig bemerkt, 60 Mm. lang und 20 Mm. breit ist. Seine obere Fläche ist matt geschliffen; der Hohlraum hat die Form eines Kugelabschnittes, einen Durchmesser von 14 Mm. und eine Tiefe von 1,5 Mm. Hartnack'sche Deckgläschen von 18 Mm. Quadrat und 0,15 Mm. Dicke lassen sich auf solchen Objectträgern sehr gut durch Oel luftdicht befestigen. Dem Tropfen auf der unteren Seite des Deckglases gab ich einen Durchmesser von ungefähr 5–7 Mm., so dass er vom Oel ringsum ungefähr noch 3–5 Mm. entfernt bleibt und dieses ihn, selbst wenn es unter dem Deckglas etwas nach innen fiesst, nicht leicht erreichen kann. Zu Kulturversuchen im Brutapparat habe ich Objectträger mit einem darauf befestigten Paraffinring sehr praktisch gefunden, man kann sich dieselben, in jeder beliebigen Grösse und Form, leicht selbst anfertigen und ganz in derselben Weise wie hohlgeschliffene Objectträger benützen.

dass sie durch mehrere Gesichtsfelder reichen; sie gleichen einem Haufen Glasfäden, welche nach Art von Schlingpflanzen sich in der verschiedensten Weise bald zu langen parallelen Zügen oder zu äusserst zierlichen spiralförmig gedrehten Bündeln vereinigen, bald aber in den unregelmässigsten Figuren zu einem unentwirrbaren Knäuel verschlingen, (p. 286) so dass es ganz unmöglich wird, den einzelnen Faden in seiner ganzen Länge weiter zu verfolgen.

Betrachtet man das freie Ende eines Fadens andauernd durch längere Zeit, etwa 15 bis 20 Minuten, dann vermag man leicht die fortwährende Verlängerung desselben direct wahrzunehmen und kann sich so das merkwürdige Schauspiel von dem sichtbaren Wachsen der Bacillen verschaffen und die unmittelbare Ueberzeugung von ihrer Weiterentwicklung gewinnen. Schon nach 10 bis 15 Stunden erscheint der Inhalt der kräftigsten und am üppigsten gewachsenen Fäden fein granulirt und bald scheiden sich in regelmässigen Abständen sehr kleine mattglänzende Körnchen ab, welche sich nach einigen weiteren Stunden zu den stark lichtbrechenden eirunden Sporen vergrössern. Allmählich zerfallen dann die Fäden, zerbröckeln an ihren Enden, die Sporen werden frei, sinken dem Gesetze der Schwere folgend in die unteren Schichten des Tropfens und sammeln sich hier in dichten Haufen an. In diesem Zustande bleibt dann das Präparat wochenlang unverändert. Die auf der Tafel XI. befindlichen Abbildungen geben ein möglichst getreues Bild (Fig. 1—4) von den eben geschilderten verschiedenen Entwicklungsstufen des *Bacillus Anthracis*.

Auch in den Präparaten, welche nach dieser Methode angefertigt und behandelt wurden, traten bisweilen verschiedenartige Bakterien in grossen Schwärmen und ruhenden Colonien als ungebetene Gäste auf und störten die Beobachtung der späteren Entwicklungsstadien des *Bacillus Anthracis*. Sobald man aber eine grössere Anzahl von Präparaten mit einiger Sorgfalt unter Anwendung von möglichst frischem, reinem *Humor aqueus* oder Blutserum und unmittelbar dem todtten Thierkörper entnommener Milzsubstanz anfertigt und in den Brütapparat bringt, wird man mindestens in der Hälfte, öfter in allen, bei wiederholter

Untersuchung eine vollkommene reine Cultur von Milzbrandbacillen finden. Bleibt unter den im Vorhergehenden angegebenen Bedingungen die Entwicklung der Bacillen ganz aus, oder wachsen letztere nur kümmerlich und kommen nicht zur Sporenbildung, dann liegt irgend ein Fehler in der Anordnung des Experimentes vor. Auf welche Kleinigkeiten es hierbei unter Umständen ankommt, mag man daraus ersehen, dass mir anfangs manche Culturen missglückten, weil ich alle Deckgläschen nach dem Gebrauch in eine Carbolsäurelösung legte und trotz sorgfältiger Reinigung durch den Geruch erkennbare Spuren von Carbolsäure bisweilen an den Gläschen haften blieben. Erst nachdem ich mich durch Controlversuche davon überzeugt hatte, dass schon so äusserst geringe (p. 287) Mengen der Carbolsäure genügten, um die Cultur der Bacillen zu stören und demgemässe die Gläschen immer durch mehrfaches Abspülen von der Carbolsäure vollständig gereinigt hatte, blieb ich von diesen Misserfolgen verschont. Später wollte es mir einmal durchaus nicht mehr gelingen, die Fäden zur Sporenbildung zu bringen; sie wuchsen in eigenthümlichen gekräuselten, ziemlich langen Formen, verkümmerten aber schliesslich, nachdem sie nur vereinzelte oder gar keine Sporen angesetzt hatten. Ich suchte vergeblich den Grund in fehlerhafter Beschaffenheit des Wärmeapparates, der Nährflüssigkeit und dergl. Endlich fiel es mir auf, dass das zum Schliessen des Präparates benutzte Oel nach flüchtigen Fettsäuren roch und als ich nun zu gleicher Zeit mehrere Präparate genau in gleicher Weise anfertigte, aber für einige ranziges Oel, für andere tadelloses Provenceröl zum Befestigen des Deckglases gebrauchte, kamen die Bacillen in letzteren zur vollkommensten Sporenbildung, in ersteren zeigten sich nur spärliche Sporen. Da mir diese Wirkung der flüchtigen Fettsäuren, oder vielleicht nur einer bestimmten Säure, welche nicht einmal direct mit dem die Bacillen enthaltenden Tropfen in Berührung kamen, sondern nur durch ein sehr geringes Quantum ihrer Dämpfe darauf einwirken konnten, sehr merkwürdig erschien, so wiederholte ich diesen Versuch zu verschiedenen Zeiten und erhielt immer dasselbe Resultat.

3. Die Sporen des *Bacillus Anthracis* entwickeln sich unter

gewissen Bedingungen (bestimmte Temperatur, Nährflüssigkeit und Luftzutritt) wieder unmittelbar zu den ursprünglich im Blute vorkommenden Bacillen. Dass die in den langen Fäden gebildeten glänzenden Körperchen in der That Sporen sind und nicht etwa zufällige Zersetzungsproducte oder Rückstände der absterbenden ausgewachsenen Bacillen, liess sich wohl schon von vorn herein nach Analogie der Entwicklungsgeschichten anderer Organismen aus der Reihe der Pilze und Algen mit Bestimmtheit annehmen. Später zu erwähnende Impfversuche mit Flüssigkeiten, welche nur Sporen von *Bacillus Anthracis* und keine Spur von Bacillen oder Fäden mehr enthielten und doch im Stande waren, mit derselben Sicherheit, wie mit frischen Bacillen Milzbrand zu erzeugen, bestätigten diese Vermuthung. Um aber einen vollständigen Einblick in den Lebenslauf des *Bacillus Anthracis* zu gewinnen und namentlich zu erfahren, ob die Sporen durch eine Zwischenform, etwa eine im Wasser lebende Schwärmspore, oder direct und in welcher Art und Weise wieder in die Bacillen übergehen, war es das Gerathenste, den einmal betretenen Weg weiter (p. 288) zu verfolgen. Womöglich musste erreicht werden, die Keimung der Sporen künstlich unter Verhältnissen vor sich gehen zu lassen, welche eine directe mikroskopische Beobachtung gestatten.

Alle Bemühungen, die Sporen in destillirtem Wasser und Brunnenwasser zur Fortentwicklung bei gewöhnlicher Temperatur oder bei 35° zu bringen, schlugen fehl. In Blutserum oder *Humor aqueus* nach der früher beschriebenen Methode in geschlossenen Zellen und im Brütapparat versuchte Culturen führten nur zu unvollkommenen Resultaten; es entwickelten sich unzweifelhafte Bacillen, welche zu langen Fäden auswuchsen und Sporen ansetzten; aber ihre Zahl war gering und der Uebergang einzelner Sporen in die Bacillen liess sich in dem Sporenhaufen nicht mit genügender Sicherheit verfolgen. Schliesslich schlug ich folgendes Verfahren ein, welches zum Ziele führte. Es wurden aus Präparaten, welche nach mikroskopischer Prüfung eine ganz reine Cultur von *Bacillus Anthracis* enthielten und nachdem die langen Fäden ganz oder grösstentheils zerfallen waren, Tröpfchen mit Sporenmassen entnommen, auf ein Deckglas gebracht

und theilweise dicht neben dem Rande desselben, theilweise mehr nach der Mitte zu schnell eingetrocknet. Dieses Eintrocknen hat den Zweck, dass die Sporenhäufchen zusammengehalten und nicht von der Nähr-Flüssigkeit auseinandergeschwemmt und zu sehr zerstreut werden. Die Sporenmassen blieben einige Stunden oder selbst Tage trocken; alsdann wurde auf einen gewöhnlichen (nicht hohl geschliffenen) Objectträger ein der Grösse des Deckglases entsprechender Tropfen *Humor aqueus* gebracht und das Deckglas so aufgelegt, dass die Sporenmassen von der Flüssigkeit benetzt wurden. Das Präparat, welches also nicht mit Oel abgeschlossen wird, kam in den früher beschriebenen feuchten Raum und mit diesem in den Brütapparat, welcher eine Wärme von 35° hatte.

Nach einer halben Stunde fingen die hier und da noch zwischen den Sporen liegenden Reste der ausgewachsenen Fäden an, vollständig zu zerfallen und nach ungefähr 1½ bis 2 Stunden waren sie verschwunden.

Schon nach 3–4 Stunden war eine Entwicklung der Sporen zu bemerken.

In den Sporenhäufchen am Rande des Deckglases war sie am weitesten fortgeschritten; denn sie hatten sich schon fast ganz in Fäden verwandelt; während nach der Mitte des Präparates zu alle Uebergänge von diesen Fäden bis zu den einfachen Sporen sich fanden. Nach Beobachtungen an zahlreichen derartigen Präparaten gestaltet sich der Vorgang bei der Sporenentwicklung folgendermassen. (p. 289)

Bei genauer Untersuchung mit Stärkeren Vergrösserungen (z. B. Hartnack immers. 9) erscheint jede Spore von eiförmiger Gestalt und in eine kuglige glashelle Masse eingebettet, welche wie ein heller schmaler, die Sporen umgebender Ring aussieht, deren kuglige Form aber beim Rollen der Sporen nach verschiedenen Richtungen leicht zu erkennen ist. Diese Masse verliert zuerst ihre Kugelgestalt, sie verlängert sich in der Richtung der Längsachse der Sporen nach der einen Seite hin und wird langgezogen eiförmig. Die Spore bleibt dabei in dem einen Pol des kleinen walzenförmigen Körpers liegen. Sehr bald wird die glashelle Hülle länger und fadenförmig und zu gleicher Zeit fängt

die Spore an ihren starken Glanz zu verlieren, sie wird schnell blass und kleiner, zerfällt wohl auch in mehrer Parteen, bis sie schliesslich ganz verschwunden ist. In Fig. 5 ist ein solcher Sporenhaufen mit den Uebergängen zu Fäden nach einem solchen Präparate wiedergegeben.

Später ist es mir auch oft gelungen in demselben Präparat und in demselben Tropfen *Humor aqueus* aus den Bacillen die Sporen und sofort aus diesen wieder eine zweite Generation von sporenhaltigen Fäden zu erziehen. Wenn nämlich nur wenige Bacillen in den Tropfen gelangten, hatte sich, wie auch sonst, ungefähr nach 20–24 Stunden die Sporenbildung vollzogen; das Nährmaterial war aber noch nicht verbraucht und einige Stunden später wuchsen die Sporen schon wieder zu Bacillen und diese zu Fäden aus.

Namentlich in derartigen Präparaten konnte der Uebergang der Sporen zu den Bacillen mit Sicherheit beobachtet werden; die Fig. 5b. ist einem solchen Präparat entnommen und Herr Prof. F. Cohn hatte die Güte, diese Zeichnung unter Anwendung einer Vergrösserung mit Seibert immers. VIII. selbst anzufertigen. Aus diesen höchst einfachen Formveränderungen der Spore bei ihrer Keimung geht also hervor, dass sie aus einem stark lichtbrechenden Tröpfchen, vielleicht einem Oel, besteht, welches von einer dünnen Protoplasmaschicht eingehüllt ist. Letztere ist die eigentliche entwicklungsfähige Zellsubstanz, während ersteres vielleicht einen bei der Keimung zu verbrauchenden Reservestoff bildet.

Mit dieser letzten Reihe von Untersuchungen ist der Kreis, welcher von den Formveränderungen des *Bacillus Anthracis* gebildet wird, geschlossen und damit die vollständige Entwicklungsgeschichte desselben gegeben.

Da in den letzten Jahren oft die wunderbarsten Beobachtungen und die widersprechendsten Ansichten über krankheitserregende *Schizophyten* veröffentlicht sind und deswegen, wie ich schon früher (p. 290) andeutete, Arbeiten dieser Art sowohl von Botanikern als Aerzten mit einem wohl berechtigten Misstrauen aufgenommen werden, so mache ich nochmals besonders darauf aufmerksam, dass es sich bei meinen Untersuchungen nicht um

eine zufällige, vereinzelte Beobachtung, sondern um möglichst oft wiederholte, mit vollständig sicherem Erfolg zu jeder Zeit anzustellende Experimente handelt.

Um Jeden, der ein Interesse für die Sache hat, in den Stand zu setzen, ohne Schwierigkeit sich selbst durch den Augenschein von der Richtigkeit des Resultates meiner Untersuchungen zu überzeugen, habe ich die oft durch mühevollen und zeitraubenden Versuche gewonnenen Methoden, nach denen ich gearbeitet habe, möglichst genau beschrieben. Ganz besonderes Gewicht lege ich übrigens noch darauf, dass Herr Prof. F. Cohn sich auf meine Bitte, der mich zu besonderem Danke verpflichtenden Mühe unterzog, meine Angaben über die Entwicklungsgeschichte des *Bacillus Anthracis* eingehend an einer Reihe von Präparaten und von mir im pflanzenphysiologischen Institut zu Breslau angestellten Experimenten zu prüfen und in allen Punkten zu bestätigen.

Die auf die Anthraxbacillen bezügliche Literatur ist mir nur theilweise zugänglich gewesen und ich muss daher auf eine vollständige Angabe derselben verzichten. Nur einige Arbeiten, welche mir erst nach Auffindung der Entwicklungsgeschichte des *Bacillus Anthracis* zur Kenntniss kamen, möchte ich mit einigen Worten berühren. Bollinger* meint, dass die Bacillen aus Reihen von Kugelbakterien zusammengesetzt sind, in welche sie gelegentlich zerfallen, und dass diese Kugelbakterien allein im Blute vorkommen, sich durch Theilung vermehren und zu Reihen vereinigt wieder Stäbchen bilden können. Fast könnte es hiernach scheinen, als ob Bollinger auch die Sporenbildung gesehen hätte. Doch ist dies nicht der Fall, denn er giebt an, nur einmal Bacillen von 0,05 Mm. Länge gesehen zu haben, eine Grösse, bei welcher die Bacillen noch nicht zur Sporenbildung kommen. Auch die l. c. p. 465 gegebene Abbildung enthält nur abgestorbene Bacillen, auf deren Form ich später zurückkomme.

Im dritten Hefte des ersten Bandes dieser Beiträge p. 200 äussert F. Cohn bei der Besprechung der eben angeführten Angaben Bollinger's, dass er die Milzbrandstäbchen dennoch für Bacillen halte und dass man nach Analogie anderer Bacillen eine Fort-

* Ziemssen's Handb. der spec. Pathol. und Therap. Bd. 3. p. 464.

pflanzung derselben durch kugelige Dauersporen erwarten müsse; eine (p. 291) Vermuthung, welche sich sehr bald verwirklicht hat. Die neueste Veröffentlichung über Milzbrandbakterien, welche von C. O. Harz herrührt, enthält nach dem mir vorliegenden Referat (Allgem. med. Centralzeitung 1876 No. 33) nur negative Resultate, welche den von mir erhaltenen positiven gegenüber ihre Bedeutung verlieren müssen.

III. *Biologie des Bacillus Anthracis*. Die Möglichkeit, den *Bacillus Anthracis* unter künstlichen Verhältnissen zu sporenhaltigen Fäden und seine Sporen wieder zu Bacillen zu entwickeln, beweist natürlich noch nicht, dass das Vorkommen des Milzbrandes unter allen Umständen auf die verschiedenen Entwicklungsformen dieser Bakterienart zurückgeführt werden müsse. Da er im lebenden Organismus, wie früher gezeigt wurde (allerdings vorläufig nur für die Thierspecies, mit welcher experimentirt wurde, beweisend), sich nicht weiter entwickelt, so kann nur durch Versuche über das Verhalten des *Bacillus Anthracis* unter Bedingungen, welchen er auf seinem muthmasslichen Wege nach dem Absterben des von ihm bewohnten Thieres unterworfen ist, eine Aufklärung hierüber gesucht werden.

Um nicht zu ausführlich zu werden, muss ich die sehr umfangreichen in dieser Richtung angestellten Versuchsreihen kurz zusammenfassen.

Substanzen, welche Milzbrandbacillen enthalten, können in trockenem Zustande oder in Flüssigkeiten suspendirt verbreitet werden. Dass sie eingetrocknet lange Zeit wirksam sein können, war schon bekannt; doch schwanken die Angaben über die Dauer dieser Wirksamkeit. Um diese letzteren genauer zu bestimmen, wurden folgende Versuche gemacht:

Milz, Lymphdrüsen, Blut von Mäusen, Kaninchen und Meerschweinchen wurden sofort, nachdem sie dem Thierkörper entnommen waren, an einem schattigen luftigen Ort getrocknet, und zwar in grösseren Stücken, in kleineren ungefähr erbsen- bis hiersckorngrossen Massen und in am Deckglase eingetrockneten dünnen Schichten. Mit diesem Material wurde anfangs täglich, später von zwei zu zwei Tagen zu gleicher Zeit, nachdem eine entsprechende Menge in *Humor aqueus* aufgeweicht war, eine

oder mehrere Mäuse geimpft und ein Culturversuch in einer Paraffinzelle gemacht. Die in sehr dünnen Lagen eingetrockneten Bacillenmassen verloren, je nach ihrer Dicke, nach 12–30 Stunden ihre Impffähigkeit und ebenso auch die Möglichkeit, im Brütapparat zu langen Fäden heranzuwachsen. Unmittelbar nach dem Anfeuchten hatten die Bacillen dasselbe Aussehen, wie im frischen Zustande; aber sie zerfielen sehr bald unter später genauer zu beschreibenden Veränderungen, sei waren also, nachdem (p. 292) sie einen gewissen Theil ihrer Feuchtigkeit verloren hatten, abgestorben. Dickere getrocknete Stücke hielten sich zwei bis drei Wochen impf- und entwicklungsfähig. Noch grössere behielten ihre Wirksamkeit, offenbar weil sie langsamer vollkommener lufttrocken werden, gegen vier bis fünf Wochen. Aber längere Zeit hindurch frisch getrocknete bacillenhaltige Massen impffähig zu erhalten, ist mir nie gelungen, obwohl ich diese Versuche in der verschiedensten Weise modificirt und wiederholt habe, weil ich, auf Davaine's Angaben mich verlassend, anfangs bestimmt glaubte, mir auf diese Weise frisch erhaltene Milzbrandsubstanzen für spätere Versuche sichern zu können; doch wurde ich stets auf das Empfindlichste getäuscht und musste meine Arbeiten deswegen mehrfach unterbrechen, bis es mir später gelang, in anderer Weise einen stets wirksamen Impfstoff zu gewinnen und mich dadurch vom Zufall unabhängig zu machen.

Auf eine Erscheinung, welche bei dieser Versuchsreihe recht auffallend hervortrat, muss ich noch besonders aufmerksam machen, dass nämlich nur solche getrocknete Substanzen Milzbrand hervorriefen, aus welchen bei den gleichzeitig angestellten Culturversuchen sich sporenhaltige Fäden entwickelten und umgekehrt. Es würde diese Beobachtung allein schon genügen, um die directe Uebertragbarkeit des Milzbrandes als von dem Vorhandensein lebensfähiger Bacillen abhängig zu beweisen.

Ehe ich zu den Versuchen über Milzbrandflüssigkeiten übergehe, muss ich eine Reihe von Culturversuchen bei verschiedenen Temperaturen erwähnen. Es war mir hauptsächlich darum zu thun, die unterste Temperaturgrenze zu finden, bei welchen der *Bacillus Anthracis* noch keimfähige Sporen zu entwickeln vermag.

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oder mehrere Mäuse geimpft und ein Culturversuch in einer Paraffinzelle gemacht. Die in sehr dünnen Lagen eingetrockneten Bacillenmassen verloren, je nach ihrer Dicke, nach 12–30 Stunden ihre Impffähigkeit und ebenso auch die Möglichkeit, im Brütapparat zu langen Fäden heranzuwachsen. Unmittelbar nach dem Anfeuchten hatten die Bacillen dasselbe Aussehen, wie im frischen Zustande; aber sie zerfielen sehr bald unter später genauer zu beschreibenden Veränderungen, sei waren also, nachdem (p. 292) sie einen gewissen Theil ihrer Feuchtigkeit verloren hatten, abgestorben. Dickere getrocknete Stücke hielten sich zwei bis drei Wochen impf- und entwicklungsfähig. Noch grössere behielten ihre Wirksamkeit, offenbar weil sie langsamer vollkommener lufttrocken werden, gegen vier bis fünf Wochen. Aber längere Zeit hindurch frisch getrocknete bacillenhaltige Massen impffähig zu erhalten, ist mir nie gelungen, obwohl ich diese Versuche in der verschiedensten Weise modificirt und wiederholt habe, weil ich, auf Davaine's Angaben mich verlassend, anfangs bestimmt glaubte, mir auf diese Weise frisch erhaltene Milzbrandsubstanzen für spätere Versuche sichern zu können; doch wurde ich stets auf das Empfindlichste getäuscht und musste meine Arbeiten deswegen mehrfach unterbrechen, bis es mir später gelang, in anderer Weise einen stets wirksamen Impfstoff zu gewinnen und mich dadurch vom Zufall unabhängig zu machen.

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nehmen im Brütapparat sehr schnell einen höchst penetranten Fäulnissgeruch an. Die Bacillen sind schon nach 24 Stunden verschwunden, ohne dass sie zu Fäden ausgewachsen wären und es gelingt dann nicht mehr, damit Milzbrand zu erzeugen. Davon dass das Absterben der Bacillen in diesem Falle weniger von dem Einfluss der sich entwickelnden Fäulnissgase, welche nicht entweichen können, sondern von dem Mangel an Sauerstoff abhängt, kann man sich leicht durch folgendes Experiment überzeugen. Ein zwischen einem gewöhnlichen Objectträger und Deckglas ohne Luftblasen befindlicher bacillenhaltiger Blutstropfen wird durch eine auf den Rand gepinselte Oelschicht luftdicht eingeschlossen und auf dem heizbaren Objecttisch erwärmt. Das Blut zeigt mit dem Mikrospektroskop untersucht anfangs die beiden Streifen des Oxyhämoglobin; dabei fangen die Bacillen ganz wie in den Zellenpräparaten, an sich zu verlängern und erreichen nach ungefähr drei Stunden die 4-5 fache Länge. Dann ist der Sauerstoff verbraucht, es verschwinden die beiden Streifen und es erscheint dafür der zwischen beiden liegende Streifen des reducirten Hämoglobin. Von diesem Zeitpunkte an hört auch das weitere Wachsthum der Bacillen vollständig auf, obwohl noch (p. 294) keine Fäulnissbakterien bemerkt werden und die eigentliche Fäulniss noch nicht eingetreten ist.* An einem solchen Präparate kann man, wenn es bei niedriger Temperatur gehalten wird, in vorzüglicher Weise die Veränderungen der Bacillen beim Absterben studiren. Dieser Vorgang gestaltet sich folgendermassen. Während frische Bacillen und im kräftigen Wachsthum befindliche (mit Ausnahme des Zeitpunktes dicht vor der Sporenbildung) immer einen homogenen glashellen Inhalt haben und nur ganz vereinzelt eine sonst nur durch winklige Knickungen angedeutete Gliederung zeigen, erkennt man in den absterbenden Bacillen als erstes Symptom eine Trübung des Inhalts und eine Sonderung desselben in kürzere Abtheilungen. Die Bacillen erscheinen dann mehr oder weniger deutlich geglie-

* Im nicht geöffneten Körper eines an Milzbrand gestorbenen Thieres verlängern sich die Bacillen, auch wenn der Cadaver längere Zeit bei einer Temperatur von 18-20° gelassen wird, nur sehr wenig oder gar nicht; offenbar weil der Sauerstoff des Blutes nach dem Tode schnell durch Oxydationsprocesse verbraucht und nicht wieder ersetzt wird.

dert, namentlich so lange noch die äusserst feine Zellenmembran diese Theile scheidernartig umhüllt und zusammenhält. Aber sehr bald verlieren die Bacillen ihre scharfen Contouren, sie scheinen aus kurzen, rundlichen, lose zusammenhängenden Stückchen zu bestehen und zerfallen schliesslich vollständig. Die mir vorliegende Abbildung Bollinger's (l. c. p. 465) ist eine ziemlich getreue Darstellung solcher abgestorbener Bacillen. Ich habe einzelne in dieser Weise zerfallende Bacillen in den verschiedensten Präparaten oft tagelang von Zeit zu Zeit beobachtet, habe aber niemals einen Uebergang derselben in Micrococcen oder dergleichen gesehen.

Ganz andere Bilder gewähren dagegen bei öfters wiederholter Untersuchung die genannten bacillenhaltigen Flüssigkeiten, wenn der Zutritt von Sauerstoff, und sei es auch nur in sehr geringer Menge, gestattet wird und ihre Temperatur nicht dauernd unter 18° herabsinkt. Sehr gut lassen sich die hierbei eintretenden Veränderungen verfolgen, wenn ungefähr 10–20 Gramm der Flüssigkeit in einem Uhrglase, auf welches eine nicht festschliessende Glasplatte aufgelegt wird, mehrere Tage bei Zimmertemperatur bleiben. Die Flüssigkeit nimmt schon nach 24 Stunden Fäulnissgeruch an, der nach weiteren 24 Stunden gewöhnlich sehr penetrant ist. Dem entsprechend finden sich auch sehr bald Micrococcen und Bakterien in grosser Menge. Daneben aber gedeiht der *Bacillus Anthracis* so gut, als ob er der alleinige Bewohner der Nährflüssigkeit wäre. Seine Fäden erreichen schon nach 24 Stunden eine beträchtliche (p. 295) Länge und haben öfters schon nach 48 Stunden und selbst noch zeitiger Spores in grosser Menge angesetzt.* Nach der Sporenentwicklung zerfallen die Fäden und die Sporen sinken zu Boden. Die Vegetation der übrigen Schizophyten, welche zufällig in die Flüssigkeit eindringen und sich darin vermehren, geht noch Tage lang in üppigster Weise weiter. Allmählich aber verschwinden auch diese, der charakteristische Fäulnissgeruch nimmt ab, schliesslich bildet sich ein schlammiger Bodensatz und

* In Paraffinzellen zu gleicher Zeit und unter denselben Verhältnissen gezüchtete Bacillen wuchsen langsamer und kümmerlicher. Vielleicht wegen des erheblich geringeren Sauerstoffvorraths.

die darüber stehende Flüssigkeit wird arm an geformten Bestandtheilen und fast klar. Sie hat zuletzt einen schwachen Geruch nach Leim oder Käse, verändert sich, wenn sie bisweilen durch den Zusatz von destillirtem Wasser vor dem Austrocknen geschützt wird, nicht mehr und ist vollständig ausgefault.

Wurden bacillenhaltige Substanzen mit destillirtem oder Brunnenwasser mässig verdünnt, dann verhindert das die Sporenbildung nicht; aber bei stärkerer Verdünnung entwickeln sich die Bacillen nicht mehr,* sie sterben bald ab und erzeugen ungefähr nach 30 Stunden eingepflicht keinen Milzbrand mehr. Die Nährflüssigkeit muss also eine gewisse noch näher zu bestimmende Menge an Salzen und Eiweiss enthalten, damit die Bacillen bis zur Sporenbildung kommen können.

Es unterliegt wohl keinem Zweifel, dass die meisten Cadaver der an Milzbrand gefallenen Thiere, welche im Sommer mässig tief eingescharrt werden, oder längere Zeit auf dem Felde, im Stalle, in Abdeckereien liegen, ebenso die blut- und bacillenhaltigen Abgänge der kranken Thiere im feuchten Boden oder im Stalldünger mindestens ebenso günstige Bedingungen für die Sporenbildung des *Bacillus Anthracis* bieten, als es in den vorher geschilderten Versuchsreihen der Fall ist. Durch diese Experimente würde also der Beweis geliefert sein, dass nicht blos durch künstliche Züchtung im Ausnahmefalle die Sporen des *Bacillus Anthracis* entstehen, sondern dass dieser Parasit in jedem Sommer im Boden, dessen Feuchtigkeit das Austrocknen der den Höhlungen des noch lebenden oder schon abgestorbenen milzbrandigen Thieres entströmenden Nährflüssigkeit verhindert, seine Keime in unzählbarer Menge ablagert.

Dass sich diese Keime im Wasser nicht verändern, aber in (p. 296) *Humor aqueus* und Blutserum wieder zu Bacillen heranwachsen, haben wir früher gesehen. Da liesse sich wohl schon von vornherein annehmen, dass, wenn von diesen Sporen auf irgend einem Wege eine oder auch mehrere in den Blutstrom eines für Milzbrand empfänglichen Thieres gelangt, hier eine neue Generation von Bacillen erzeugt wird. Um diese Annahme auch

*z.B. Bacillen in Mausemilz mit dem zwanzigfachen Quantum destillirten Wassers verdünnt, wuchsen nicht.

experimentell zu prüfen, wurden noch folgende Versuche angestellt.

Von zwei mit bacillenhaltigen Blutserum gefüllten, verdeckten Uhrgläsern blieb das eine im Zimmer, das andere wurde in einem kalten Raume (8°) aufbewahrt und von beiden täglich zwei Thiere geimpft. Im Blutserum, welches kalt stand, fingen die Bacillen am dritten Tage an körnig und gegliedert zu werden, bis dahin war es wirksam; die später damit geimpften Thiere blieben gesund. Die Impfungen mit dem warmstehenden Blutserum waren vor und nach der Sporenbildung in den Fäden des *Bacillus Anthracis* wirksam; selbst nach 14 Tagen liess sich mit solchem gefaulten Blute, welches Bacillen-Sporen enthält, noch mit derselben Sicherheit Milzbrand erzeugen, wie mit frischer stäbchenhaltiger Milz. Die Sporen scheinen sich sehr lange Zeit in faulenden Flüssigkeiten ebenso gut, wie in nicht faulenden, keimfähig zu erhalten. Denn mit Glaskörper von Rinderaugen, in welchem ich bei ungefähr 20° Bacillen aus einer Mausemilz zur Sporenbildung kommen liess und welcher nach drei Wochen vollständig ausgefault war, konnte noch nach elf Wochen mit absoluter Sicherheit durch Impfung Milzbrand hervorgerufen werden. Der Bodensatz dieser ausgefaulten Flüssigkeit enthielt sehr viele von kleinen Schleimflocken zusammengehaltene Bacillen-Sporen, während man in der fast klaren Flüssigkeit bei mikroskopischer Untersuchung oft mehrere Gesichtsfelder durchsuchen musste, ehe man einige vereinzelte Sporen fand. Von Fäden war natürlich nicht das Geringste mehr vorhanden. Bei den Impfungen mit dem sporenreichen Bodensatz und mit der sporenen Flüssigkeit stellte sich die interessante Thatsache heraus, dass mit ersterem also mit vielen Sporen geimpfte Mäuse nach 24 Stunden, mit letzterer also mit weniger Sporen geimpfte Mäuse nach drei bis vier Tagen an Milzbrand starben. Ich bemerke noch besonders, dass ich diesen Versuch mehrere Male und immer mit demselben Erfolg wiederholt habe.

Sporenhaltige Flocken derselben Flüssigkeit wurden drei Wochen in einem mitt Brunnenwasser gefüllten offenen Reagensglase aufbewahrt; trotzdem blieben dieselben wirksam bei der damit vorgenommenen Impfung.

(p. 297) Ebensolche sporenhaltige Substanzen wurden getrocknet, nach einiger Zeit mit Wasser wieder aufgeweicht und dieser Procedur wiederholt unterworfen; aber sie verloren ihre Fähigkeit Milzbrand zu erzeugen, dadurch nicht.

Hiernach wird es nun auch leicht erklärlich, warum die Meinungen der Experimentatoren über die Wirksamkeit des getrockneten Milzbrandblutes so weit auseinandergehen; da der Eine frisches, schnell getrocknetes Blut benutzte, welches keine Sporen enthielt und, wie ich früher gezeigt habe, sich höchstens fünf Wochen wirksam erhält; von Anderen dagegen wurde mit Blut geimpft, das langsam bei Zimmer- oder Sommer-Temperatur eingetrocknet war und in welchem sich Sporen gebildet hatten. Ich besitze eine kleine Sammlung von Milzbrandsubstanzen, welche unter den verschiedensten Umständen und zu verschiedenen Zeiten getrocknet und in unverstöpselten, enghalsigen Gläsern aufbewahrt sind. Als ich auf die Bedeutung der Sporen in getrockneten Milzbrandmassen aufmerksam wurde, untersuchte ich diese getrockneten Blut-, Milz- und Drüsenstückchen nochmals genau auf ihre Fähigkeit, mit *Humor aqueus* aufgeweicht in Glaszellen die charakteristischen sporenhaltigen Fäden des *Bacillus Anthracis* und bei der Impfung Milzbrand entstehen zu lassen. Hierbei stellte sich heraus, dass die in kleinen Stücken schnell getrockneten Theile keine Sporen enthielten und weder Fäden noch Milzbrand hervorzubringen vermochten. Schafmilz dagegen, welche in grösseren Stücken im Zimmer langsam getrocknet war, und einige Blutproben, welche in grösseren Quantitäten aufgestellt gewesen waren und mehrere Tage zum vollständigen Eintrocknen gebraucht hatten, enthielten zahlreiche mehr oder weniger freie Sporen und Bruchstücke von sporenhaltigen Fäden. Alle diese sporenhaltigen Substanzen riefen nach der Einimpfung Milzbrand hervor und entwickelten in Nährflüssigkeiten oft die schönsten sporenhaltigen Fäden von *Bacillus Anthracis*. Wie lange sich die getrockneten Sporen keimfähig halten, lässt sich zur Zeit nicht mit Bestimmtheit angeben; wahrscheinlich wird dieser Zeitraum eine längere Reihe von Jahren umfassen; wenigstens habe ich mit Schafblut, welches vor fast vier Jahren getrocknet

ist, noch in letzter Zeit vielfach Impfungen ausgeführt, welche ausnahmslos tödtlichen Milzbrand bewirkten.*

Mehrfach ist die Identität der durch Impfungen mit Milzbrandblut hervorgerufenen Krankheit mit Septicämie und ebenso das (p. 298) umgekehrte Verhältniss behauptet worden. Um diesen Einwand, der möglicherweise auch meinen mit faulenden Milzbrandsubstanzen angestellten Impfversuchen gemacht werden könnte, zu begegnen, habe ich mit faulendem Blute von gesunden Thieren mit bacillenfreiem faulenden *Humor aqueus* und Glaskörper Mäuse mehrfach geimpft. Dieselben blieben fast immer gesund, nur zwei Mäuse starben von zwölf geimpften, und zwar einige Tage nach der Impfung; sie hatten vergrösserte Milz, aber diese sowohl wie das Blut waren vollständig frei von Bacillen. Ferner wurden Thiere mit faulendem Glaskörper geimpft, in welchem sich eine dem *Bacillus Anthracis* sehr ähnliche Bacillusart spontan entwickelt hatte. Die Sporen der beiden Bacillusarten waren weder in Grösse noch sonstigem Aussehen von einander zu unterscheiden; nur die Fäden des Glaskörper-Bacillus waren kürzer und deutlich gegliedert. Alle Impfungen mit diesen mehrmals von mir auf Glaskörper gefundenen Bacillen und mit ihren Sporen vermochten keinen Milzbrand zu erzeugen. Auch solche Thiere, welche mit Sporen der im Heu-Infus von Prof. F. Cohn gezüchteten Bacillen geimpft wurden, blieben gesund. Dagegen habe ich mehrfach mit Sporenmassen, welche in Glaskzellen gezüchtet waren und wie ich mich vorher durch mikroskopische Untersuchungen versicherte, aus ganz reinen Culturen von *Bacillus Anthracis* stammten, geimpft und jedesmal starben die geimpften Thiere an Milzbrand. Es folgt hieraus, dass nur eine Bacillusart im Stande ist, diesen specifischen Krankheitsprocess zu veranlassen, während andere Schizophyten durch Impfung gar nicht oder in anderer Weise krankheitserregend wirken. Es könnte auffallend erscheinen, dass von meinen mit faulendem Blute geimpften Versuchsthieren nur ausnahmsweise

* Die beim Bearbeiten von Häuten, Haaren und dergl. entstandenen Milzbrandkrankungen bei Menschen, können, wenn diese Gegenstände schon vor Jahren getrocknet sind, nur durch sporenhaltige Staubtheile veranlasst sein.

eins an Septicämie zu Grunde ging; dem gegenüber bemerke ich, dass ich nicht, wie es gewöhnlich üblich ist, das faulende Blut nach Cubikcentimeteren einspritzte, sondern nur eine verschwindend kleine Menge desselben dem Körper des Thieres einimpfte und damit natürlich die Wahrscheinlichkeit, die im Blute vielleicht sparsam vorhandenen septisch wirkenden Formelemente in den Blutstrom zu bringen, sehr verringert wird.

Dass die Sporen des *Bacillus Anthracis* Milzbrand hervorrufen, wenn sie direkte in den Säftestrom des Thierkörpers gebracht werden, ist durch die zuletzt besprochenen Versuche wohl hinreichend bewiesen. Die Sporen müssen also wirksam werden, sobald sie in getrocknetem Zustande als Staubpartikelchen oder in Flüssigkeiten suspendirt auf Wunden, wenn diese auch noch so klein sind, gelangen. Man dürfte wohl kaum eines unsrer Hausthiere finden, dessen Haut (p. 299) nicht mit einigen Kratzwunden oder kleinen durch Scheuern, Reiben und dergl. entstandenen Hautabschärfungen versehen ist und damit dem gefährlichen Schmarotzer einen bequemen Eingang darbietet. Trotzdem ist damit noch nicht gesagt, dass die Milzbrandsporen nur auf diesem Wege einzuwandern vermögen. Es müssen, um die Milzbrandätiologie vollständig zu haben, auch die Verdauungswege und die Respirationsorgane auf ihre Resorptionsfähigkeit für Milzbrandbacillen und deren Sporen untersucht werden.

Um zu sehen, ob das Milzbrandcontagium vom Verdauungskanal aus in den Körper eindringen kann, habe ich zuert Mäuse mehrere Tage lang mit frischer Milz von Kaninchen und vom Schaf, welche an Milzbrand gestorben waren, gefüttert. Mäuse sind ausserordentlich gefräßig und nehmen in kurzer Zeit mehr als ihr Körpergewicht beträgt, an milzbrandigen Massen auf, so dass also ganz erhebliche Mengen von Bacillen den Magen und Darm der Versuchsthiere passirten. Aber es gelang mir nicht, dieselben auf diese Weise zu inficiren. Dann mangle ich den Thieren sporenhaltige Flüssigkeit unter das Futter; auch das frassen sie ohne jeden Nachtheil; auch durch Fütterung grösserer Mengen von sporenhaltigem, kurz vorher oder schon vor Jahren getrocknetem Blute konnte kein Milzbrand bei ihnen erzeugt

werden. Kaninchen, welche zu verschiedenen Zeiten mit sporenhaltigen Massen gefüttert wurden, blieben ebenfalls gesund. Für diese beiden Thierspecies scheint demnach eine Infection vom Darmkanal aus nicht möglich zu sein.

Ueber das Verhalten der mit Staub in die Athmungsorgane gelangten Sporen vermag ich bis jetzt nichts anzugeben, da es mir noch nicht möglich war, darauf bezügliche Versuche anzustellen.

Ich schliesse hier noch einige Versuchsreihen und Beobachtungen an, welche nicht direct mit der Aetiologie des Milzbrandes in Verbindung stehen, aber doch Interesse genug bieten, um mitgetheilt zu werden.

Den schon von Brauell gemachten Versuch, sowohl mit dem bacillenhaltigen Blute trächtiger Thiere, als mit dem bacillenfren Blute des Fötus derselben zu impfen, habe ich mit einem trächtigen Meerschweinchen und zwei trächtigen Mäusen wiederholt. Das Resultat war das nämliche, wie bei dem Experiment von Brauell; die mit dem mütterlichen Blute geimpften Thiere starben an Milzbrand, die mit dem fötalen Blute geimpften blieben gesund. Um zu sehen, wie bald nach der Impfung die ersten Bacillen im Blute oder in der Milz der geimpften Thiere sich efinden, wurden neun Mäuse zu gleicher Zeit geimpft. Nach zwei, vier, sechs, acht, zehn, zwölf, (p. 300) vierzehn und sechzehn Stunden wurde jedesmal eine dieser Mäuse durch Chloroform getödtet und Blut sowohl als Milz sofort untersucht. In den sechs ersten Thieren wurden keine Bacillen gefunden. Erst in der Milz der vierzehn Stunden nach der Impfung getödteten Maus zeigten sich vereinzelte Bacillen. Bei der Maus, welche sechzehn Stunden gelebt hatte, fanden sich schon mehr Bacillen und die Milz war vergrössert. Die letzte starb nach siebzehn Stunden unter den gewöhnlichen charakteristischen Symptomen; ihre Milz war erheblich vergrössert und vollgestopft mit dichten Bacillenmassen. Das Eindringen der Bacillen in den Blutstrom scheint also langsam vor sich zu gehen, aber wenn sie erst einmal hineingelangt sind und hier in ihrer eigentlichen Heimath festen Fuss gefasst haben, vermehren sie sich in der üppigsten Weise.

Ausser an Mäusen, Kaninchen und Meerschweinchen habe

ich Impfversuche an zwei Hunden, einem Rebhuhn und einem Sperling gemacht. Obwohl ich diese Thiere wiederholt mit ganz frischem Material impfte, so ist es mir doch nicht gelungen, sie mit Milzbrand zu inficiren.

Auch Frösche sind ganz unempfänglich für Impfungen mit *Bacillus Anthracis* oder dessen Sporen. Als ich einigen Fröschen grössere Stücke Milz von an Milzbrand gestorbenen Mäusen unter die Rückenhaut brachte, die Thiere nach 48 Stunden tödtete und untersuchte, stellte sich folgender bemerkenswerthe Befund heraus. Das Blut der Frösche war vollkommen frei von Bacillen. Die Mausemilz war mit ihrer Umgebung leicht verklebt und hatte statt ihrer dunkelbraunrothen Farbe eine mehr hellgrau-rothe angenommen. Bei der mikroskopischen Untersuchung derselben finden sich in der Mitte noch unveränderte Bacillen in grosser Menge, aber in den äusseren Schichten trifft man auf viele Bacillen, welche dicker geworden sind und sich verlängert haben, und zwischen diesen sieht man eigenthümliche Gebilde in grosser Zahl; nämlich mehr oder weniger regelmässig spiralförmig gewundene Bacillen, welche theils frei sind, theils aber auch von einer sehr dünnwandigen Kapsel eingeschlossen werden. Die Erklärung für diese ungewöhnliche Gestaltung der Bacillen ist leicht zu finden, wenn man die fast gallertartige, anscheinend von der Froschhaut ausgeschiedene äusserste Umhüllungsschicht der Milz untersucht (Fig. 7). Diese Schicht besteht aus grossen, in eine strukturlose zähflüssige Grundsubstanz eingebetteten Zellen, welche fast die Grösse Grundsubstanz eingebetteten Zellen, welche fast die Grösse der Froschblutkörperchen erreichen (Fig. 7a). Dieselben sind trotz ihrer Grösse sehr blass und zart, haben einen sehr deutlichen Kern mit Kernkörperchen und enthalten viele sehr kleine, (p. 301) in lebhaftester Molekularbewegung befindliche Körnchen. In den meisten von diesen Zellen nun befinden sich einzelne oder mehrere Kurze gerade Bacillen, in anderen etwas gekrümmte, geknickte, zu Haufen und Bündeln vereinigte und vorzugsweise spiralförmig gedrehte Bacillen (Fig. 7b). Sobald die Zellen mehrere Bacillen beherbergen, erscheinen die Molekularkörnchen in ihnen vergrössert, nimmt aber die Bacillenwucherung in ihnen überhand, dann ver-

schwinden diese Körnchen und zuletzt auch der noch am längsten zu erkennende Kern. Dass die als kurze Stäbchen von den Zellen aufgenommenen Bacillen in diesen wachsen und, nachdem sie das Innere derselben unter Bildung von verschiedenen Knickungen und Krümmungen ausgefüllt haben, schliesslich sprengen, geht daraus hervor, dass man neben den freigerwordenen Bacillen-Spiralen (Fig. 7g) und -Bündeln zusammengefallene und leere Zellmembranen als letzten Rest der zerstörten Zellen findet (Fig. 7c).*

Ganz besonders schön sind diese bacillenhaltigen Zellen zu sehen, wenn dem Präparat etwas destillirtes Wasser zugesetzt wird. Die Zellen quellen dadurch etwas auf, ihr Inhalt wird deutlicher und wenn sie durch die Flüssigkeitsströmungen fortgerissen in eine rollende Bewegung versetzt werden, kann man sich leicht die Ueberzeugung verschaffen, dass auch einzelne Bacillen wirklich im Innern der Zelle und zwar gewöhnlich dicht neben dem Kern liegen und nicht etwa nur in die weiche Zelloberfläche eingedrückt sind. Man hat schon vielfach die Vermuthung ausgesprochen, dass die amöboiden Zellen des Thierkörpers, also vor Allem die weissen Blutkörperchen in derselben Weise, wie sie den leicht nachweisbaren künstlich ins Blut eingeführten Farbekörnchen den Eingang in ihr Protoplasma gestatten, so auch die in die Blutbahn eingedrungenen Micrococci aufzunehmen vermögen. So viel ich weiss, ist es jedoch bis jetzt nicht gelungen, die weder durch ihre Form noch durch ihre Reactionen von den Molekularkörnchen dieser Zellen scharf unterschiedenen Micrococci als solche mit Bestimmtheit nachzuweisen. Auch scheint bis jetzt überhaupt kein vollkommen sicheres Beispiel für das Vorkommen von schizophytenhaltigen lebenden thierischen Zellen bekannt zu sein, und ich habe deswegen von den vorhin beschriebenen Zellen in (p. 302) Fig. 7 eine Abbildung gegeben. Diese Beobachtung steht in sofern nicht

* Zu mehr als mittlerer Länge wachsen die Fäden unter der Froshhaut nicht aus, ich habe auch niemals Sporenentwicklung in denselben gesehen. Nach mehreren Tagen wird ihre Zahl geringer, die scheinen allmählich zu zerfallen, doch habe ich bei einem Frosche zehn Tage nach Transplantation der Mausemilz noch lange Fäden und bacillenhaltige Zellen gefunden.

vereinzelt, als ich bei andern Fröschen, nachdem faules getrocknetes Blut unter die Rückenhaut gebracht war, dieselben Zellen gefunden habe; aber in diesem Falle enthielten sie ganz andere kurzgliederige Bacillen, welche meistens mit einer Dauerspore versehen waren (Billroth's Helobacterien). Auch in der frisch untersuchten Milz eines an Milzbrand gefallenen Pferdes (die einzige, welche ich zu untersuchen Gelegenheit hatte) waren neben sehr zahlreichen freien Stäbchen grosse blasse Zellen, meistens mit mehreren Kernen vorhanden, von denen viele eine, bis zehn und mehr Bacillen enthielten.

IV. Aetiologie des Milzbrandes. Werfen wir nun einen Blick zurück auf die bis jetzt gewonnenen Thatsachen und versuchen wir mit ihrer Hülfe die Aetiologie des Milzbrandes festzustellen, so dürfen wir uns nicht verhehlen, dass zur Construction einer lückenlosen Aetiologie noch Manches fehlt. Vor Allem ist nicht zu vergessen, dass sämmtlich Thierexperimente an kleinen Nagethieren angestellt sind. Es ist allerdings unwahrscheinlich, dass die Wiederkäuer, die eigentlichen Wohnthiere des uns beschäftigenden Parasiten, sich diesem gegenüber sehr verschieden von Nagethieren verhalten sollten. Aber schon bei den Impfversuchen besteht in sofern ein Unterschied, dass kleine Thiere nach 24–30 Stunden, grosse erst nach mehreren Tagen sterben. Könnten nicht vielleicht während dieser längeren Zeit die Bacillen an irgend einer Stelle des thierischen Körpers zur Sporenbildung kommen? Oder gelangen sie überhaupt niemals im lebenden Körper zur Ansetzung von Sporen? Ferner sind die Fütterungsversuche mit Bacillen und Sporen bei Nagethieren mit ihrem negativen Resultat durchaus nicht massgebend für Wiederkäuer, deren ganzer Verdauungsprozess doch wesentlich anders ist. Einathmungsversuche mit sporenhaltigen Massen fehlen noch ganz. Auch sind Versuche über das Verhalten grösserer Milzbrandcadaver bei verschiedenen Temperaturen, in verschiedenen Bodentiefen und Bodenarten (Thon-, Kalk-, Sandboden, trockener Boden, feuchter Boden, Einfluss der Grundwassers) in Bezug auf die Sporenbildung der Bacillen noch nicht gemacht und es würde doch von höchstem praktischem Werth sein, gerade hierüber sichere Kenntniss zu erlangen. Noch eine Menge Ein-

zelheiten über das Verhalten der Bacillen und ihrer Sporen gegen zerstörende oder ihre Entwicklung hindernde Stoffe, über den Vorgang ihrer Einwanderung in die Blut- und Lymphgefäße müssten erforscht werden. Wenn aber auch noch manche Frage über diesen bisher so räthselhaften Parasiten zu lösen (p. 303) ist, so liegt sein Lebensweg jetzt doch so weit vor uns offen, dass wir die Aetiologie der von ihm veranlassten Krankheit wenigstens in der Grundzügen mit voller Sicherheit feststellen können.

Vor der Thatsache, dass Milzbrandsubstanzen, gleichviel ob sie verhältnissmässig frisch oder ausgefault oder getrocknet und Jahre alt sind, nur dann Milzbrand zu erzeugen vermögen, wenn sie entwicklungsfähige Bacillen oder Sporen des *Bacillus Anthracis* enthalten, vor dieser Thatsache müssen alle Zweifel ob der *Bacillus Anthracis* wirklich die eigentliche Ursache und das Contagium des Milzbrandes bildet, verstummen. Die Uebertragung der Krankheit durch feuchte Bacillen im ganz frischen Blut kommt in der Natur wohl nur selten vor, am leichtesten noch bei Menschen, denen beim Schlachten, Zerlegen, Abhäuten von milzbrandigen Thieren Blut oder Gewebssaft in Wunden gelangt. Häufiger wird wahrscheinlich die Krankheit durch getrocknete Bacillen veranlasst, welche, wie nachgewiesen wurde, ihre Wirksamkeit einige Tage, im günstigsten Falle gegen fünf Wochen erhalten können. Durch Insekten, an Wolle und dergleichen haftend, namentlich mit dem Staub, können sie auf Wunden gelangen und dann die Krankheit hervorrufen. Bacillenhaltige Massen, welche in Wasser gelangen und dort stark verdünnt werden, verlieren sehr bald ihre Wirksamkeit und tragen zur Verbreitung des Milzbrandes wahrscheinlich nur ausnahmsweise bei.

Die eigentliche Masse der Erkrankungen aber, welche fast immer unter solchen Verhältnissen eintritt, dass die eben genannten Uebertragungsweisen ausgeschlossen werden müssen, kann nur durch die Einwanderung von Sporen des *Bacillus Anthracis* in den Thierkörper verursacht werden. Denn die Bacillen selbst können sich in dauernd trockenem Zustande nur kurze Zeit lebensfähig erhalten und vermögen deswegen sich weder im feuchten Boden zu halten, noch den wechselnden Witterungsverhältnissen (Niederschlägen, Thau) Widerstand zu leisten, wahr-

end die Sporen dagegen in kaum glaublicher Art und Weise ausdauern. Weder jahrelange Trockenheit, noch monatelanger Aufenthalt in faulender Flüssigkeit, noch wiederholtes Eintrocknen und Anfeuchten vermag ihre Keimfähigkeit zu stören. Wenn sich diese Sporen erst einmal gebildet haben, dann ist hinreichend dafür gesorgt, dass der Milzbrand auf lange Zeit in einer Gegend nicht erlischt. Dass aber die Möglichkeit zu ihrem Entstehen oft genug gegeben ist, wurde früher schon hervorgehoben. Ein einziger Cadaver, welcher unzweckmässig behandelt wird, kann fast unzählige Sporen liefern und wenn auch Millionen von diesen Sporen schliesslich zu Grunde gehen ohne zur Keimung im Blute (p. 304) eines Thieres zu gelangen, so ist bei ihrer grossen Zahl doch die Wahrscheinlichkeit nicht gering, dass einige vielleicht nach langer Lagerung im Boden oder im Grundwasser, oder an Haaren, Hörnern, Lumpen und dergleichen angetrocknet als Staub, oder auch mit Wasser auf die Haut der Thiere gelangen und hier direct durch eine Wunde in die Blutbahn eintreten, oder auch später durch Reiben, Scheuern und Kratzen des Thieres in kleine Hautabschilferungen eingerieben werden. Möglicherweise dringen sie auch von den Luftwegen oder vom Verdauungskanal aus in die Blut- oder Lymphgefässe ein.

Wenn es nun gelungen ist, die Art und Weise der Verbreitung des Milzbrandes und die Bedingungen aufzufinden, unter denen das Contagium sich immer wieder von Neuem erzeugt, sollte es da nicht möglich sein, unter Berücksichtigung jener Bedingungen das Contagium, also den *Bacillus Anthracis*, in seiner Entwicklung zu hindern und so die Krankheit auf ein möglichst geringes Mass zu reduciren, vielleicht sogar gänzlich auszurotten? Dass diese Frage ein nicht geringes Interesse beansprucht, mag daraus hervorgehen, dass nach Spinola* ein einziger preussischer Kreis (Mannsfelder Seekreis) jährlich für 180,000 Mk. Schafe durch Milzbrand verliert, dass allein im Gouvernement Nowgorod in den Jahren 1867–1870 über 56,000 Pferde, Kühe und Schafe und ausserdem 528 Menschen an Milzbrand zu Grunde gingen.†

Die jetzt bestehenden Massregeln gegen den Milzbrand be

* Pappenheim, Sanitätspolizei Band II. p. 276.

† Grimm (Virchow's Archiv B. 54 p. 262) citirt nach Bollinger l. c. p. 469.

schränken sich auf Anzeigepflicht, Vergraben der Cadaver in mässig tiefen Gruben, Desinfection und Absperrung des von der Seuche befallenen Ortes. Ganz abgesehen davon, dass erfahrungsgemäss wegen der höchst lästigen Sperrmassregeln die wenigsten Milzbrandfälle angezeigt werden und dass der gerade unter den Schafen am meisten verbreitete Milzbrand fast ganz unbeachtet bleibt und vernachlässigt wird, so muss offenbar das Eingraben der Cadaver in den feuchten Erdboden die Bildung von Sporen und damit die Fortpflanzung des Contagiums eher fördern als dieselbe verhindern. Bis jetzt ist es anscheinend auch noch nirgends wo gelungen, auf diese Weise den Milzbrand dauernd zu beseitigen. Im Gegentheil hat Oemler* seinen Schafverlust an Milzbrand von 21% pro anno auf 2% herabgebracht, nachdem er das (p. 305) Verscharren aller Cadaver ohne Ausnahme auf Feldern und Weiden auf das Strengste untersagt hatte.

Wir müssen uns also nach anderen Mitteln umsehen, um die Heerden von diesem Würgeengel zu befreien und tausende von Menschen vor einem qualvollen Tode zu schützen.

Das sicherste Mittel wäre, alle Substanzen, welche *Bacillus Anthracis* enthalten, zu vernichten. Da es aber nicht ausführbar ist, diese Menge von Cadavern, wie sie der Milzbrand liefert, durch Chemikalien oder Siedehitze unschädlich zu machen, oder gar durch Verbrennen aus dem Wege zu schaffen, so müssen wir auf dieses Radicalmittel verzichten. Wenn es aber auch nur gelänge, die Entwicklung der Bacillen zu Sporen zu verhindern oder wenigstens auf ein Minimum zu reduciren, dann müssten schon die Milzbrand-Erkrankungen immer mehr und mehr abnehmen und schliesslich verschwinden.

Da die Bacillen, wie wir gesehen haben, zur Sporenbildung Luftzufuhr, Feuchtigkeit und eine höhere Temperatur als ungefähr 15° nöthig haben, so muss es genügen, ihnen eine dieser Bedingungen zu nehmen, um sie an der Weiterentwicklung zu hindern. Die schnelle Austrocknung grosser Cadaver würde besondere Apparate erfordern und selbst grössere Schwierig-

* Bollinger l. c. p. 453.

keiten machen, als das Verbrennen. Dagegen könnte man ohne erhebliche Mühe und Kosten die Milzbrand-Cadaver längere Zeit, auch selbst im Sommer, unter 15° abkühlen, ihnen gleichzeitig den Sauerstoffzutritt beschränken und auf diese Weise die Bacillen zum Absterben bringen. Wenn man nämlich bedenkt, dass im mittleren Europa, also namentlich in Deutschland in einer Boden-Tiefe von 8–10 Metern eine fast constante Temperatur herrscht, welche dem Jahresmittel sehr nahe kommt, also auf jeden Fall unter 15° C. bleibt, so brauchte man nur geräumige Brunnen oder Gruben von dieser Tiefe anzulegen und die Milzbrandcadaver darin zu versenken, um die Bacillen zu vernichten und die Cadaver dadurch unschädlich zu machen. Je nach der Durchschnitts-Zahl der Milzbrandfälle müssten derartige Gruben in geringer oder grosser Zahl für bestimmte Bezirke gemacht werden. Dieselben würden sich in mässiger Entfernung von den Wirthschaftsgebäuden befinden und natürlich mit einem sicheren Verschluss zu versehen sein. Man würde dadurch zugleich den nicht zu unterschätzenden Vortheil erlangen, dass nicht, wie es jetzt gewöhnlich geschieht und wie ich aus eigener Erfahrung weiss, die vorschriftsmässig oder auch vorschriftswidrig vergrabenen Milzbrandcadaver regelmässig von Dieben (oft genug von denselben Leuten, (p. 306) welche sie am Tage eingescharrt haben) des Nachts wieder herausgeholt, zertheilt und überall hin verschleppt werden.

Vielleicht verhindert auch der Einfluss gewisser Bodenarten oder ein gewisser Feuchtigkeitsmangel und tiefer Grundwasserstand die Sporenentwicklung, worauf das an bestimmte Gegenden gebundene Vorkommen des Milzbrandes und die Abnahme desselben nach ausgedehnten Meliorationen und Entwässerungen hindeutet.

Der von Buhl berichtete Fall,* dass Milzbrand unter Pferden auf dem Gestüte Neuhof bei Donauwörth vollkommen aufhörte, als man auf den Rath v. Pettenkofer's den Stand des Grundwassers durch Drainage herabgesetzt hatte, würde gleichfalls hierher gehören.

* Bollinger l. c. p. 455.

Auf jeden Fall ist die Möglichkeit, die Entwicklung der Milzbrandsporen zu verhüten, gegeben und das grosse Interesse, welches diese Angelegenheit beansprucht, müsste zu weiteren Versuchen in der angegebenen Richtung auf geeigneten Versuchsstationen dringend auffordern.

Eine Wahrnehmung, welche ich in hiesiger Gegend über das Vorkommen des Milzbrandes gemacht habe, schliesse ich hier noch an, weil dieselbe für die Milzbrandprophylaxis wohl zu berücksichtigen ist. Es ist nämlich auffallend, dass der Milzbrand das ganze Jahr hindurch fast ohne Unterbrechung unter den Schafen herrscht. In den grösseren Heerden fallen fast niemals viele Schafe auf einmal, sondern gewöhnlich einzelne oder wenige in Zwischerräumen von einigen Tagen oder Wochen. Rinder werden weit seltener und nur in grossen Pausen befallen, so dass öfters mehrere Monate, ein halbes Jahr und noch längere Zeit zwischen den einzelnen Fällen liegen. Bei Pferden tritt Milzbrand hier nur ganz ausnahmsweise auf. Es scheint demnach, dass das Schaf das eigentliche Woonthier des *Bacillus Anthracis* ist und dass er nur unter besonderen Verhältnissen gelegentlich Excursionen auf andere Thierarten macht. Für diese Ansicht spricht auch die Beobachtung von Leonhardt,* dass in Bönstadt, welches sehr viel durch Milzbrand litt, derselbe unter den Rindern fast vollkommen erlosch, nachdem man die Schafe abgeschafft hatte, welche im Sommer massenhaft an Milzbrand fielen. Es folgt aber daraus, dass bei allen Massregeln gegen die Seuche der Milzbrand unter den Schafheerden die meiste Beachtung verdient.

V. Vergleich des Milzbrandes mit anderen Infections-Krankheiten. Damit, dass der Milzbrand auf seine eigentlichen Ursachen zurückgeführt wurde, ist es gleichzeitig zum ersten Male gelungen, (p. 307) Licht über die Aetiologie einer jener merkwürdigen Krankheiten zu verbreiten, deren Abhängigkeit von Bodenverhältnissen genügend aufzuklären weder den Anstrengungen der Forschung, noch den kühnsten und verwickeltsten Hypothesen bislang möglich gewesen ist. Es liegt deswegen sehr nahe, einen Vergleich zwischen Milzbrand und den durch ihre Verbreitungsweise ihm nahestehenden Krankheiten, vor Allem mit Typhus und Cholera anzustellen.

* Bollinger l. c. p. 453.

Mit Typhus hat der Milzbrand Aehnlichkeit durch die Abhängigkeit vom Grundwasser, durch die Vorliebe für Niederungen, durch das über das ganze Jahr vertheilte sporadische Auftreten und das daneben eintretende Anschwellen der Erkrankungsfälle zur Epidemie im Spätsommer. Die ersten der oben genannten Punkte treffen auch für die Cholera zu; in einer Hinsicht aber stimmt das Contagium der Cholera mit dem des Milzbrandes in so eigenthümlicher Weise zusammen, dass wohl die Annahme eines reinen Zufalls ausgeschlossen werden muss. v. Pettenkofer hat darauf hingewiesen, dass das Cholera-Contagium auf Schiffen, wenn diese kein Land berühren, meist in drei bis vier Wochen abstirbt, nur wenn dasselbe vor dieser Zeit wieder in geeigneten Boden gelangt, vermag sich die Krankheit weiter zu verbreiten. Nehmen wir nun einmal an, dass der Milzbrand eine Krankheit wäre, welche in Indien heimisch ist, und dass von dieser Krankheit befallene Thiere nur nach vier- bis fünfwöchentlicher Seefahrt zu uns gelangen könnten, dann würde gerade so wie bei der Cholera eine Verschleppung auf dem Seewege nicht möglich sein, da sich aus Mangel an feuchtem Boden keine Sporen bilden könnten und die etwa an Gegenständen eingetrockneten Bacillen schon vor Beedigung der Fahrt abgestorben wären. Würden wir noch ferner annehmen, dass der Milzbrand eine Krankheit sei, die nicht durch grosse Bacillen, sondern durch andere ausserordentlich kleine, an der Grenze des Sichtbaren stehende Schizophyten erzeugt werde, welche nicht frei im Blute, sondern (wie die Bacillen in der Pferdemitz) in den weissen Blutkörperchen, in den Zellen der Lymphdrüsen und der Milz versteckt, ihre deletäre Wirkung ausübten, dann müsste man diesen Schizophyten eine noch viel nähere Verwandtschaft mit dem Contagium der Cholera und des Typhus zugestehen. Keine Substanz könnte in der That eine grössere Aehnlichkeit mit dem Contagium dieser Krankheit besitzen, als ein derartiges Milzbrandcontagium.

Bei solchen Betrachtungen regt sich unwillkürlich die Hoffnung, dass auch das Typhus- und Cholera-Contagium in Form von Kugelbakterien oder ähnlichen Schizophyten aufzufinden sein müsse. Dem (p. 308) stehen jedoch die erheblichsten Bedenken

entgegen. Vorausgesetzt nämlich, dass diese Krankheiten von einem belebten Contagium abhängen, so muss angenommen werden, dass dasselbe unsern optischen Hilfsmitteln schwer oder gar nicht zugänglich ist, da viele der geübtesten Mikroskopiker es bis jetzt vergeblich gesucht haben. Sollte ein derartiges Contagium noch gefunden werden, dann würde uns ausserdem, da Typhus und Cholera nicht auf Thiere zu übertragen ist, das einzige Mittel fehlen, um uns stets von der Identität der möglicherweise in ihrer äusseren Gestalt wenig charakteristischen Schizophyten zu überzeugen. Also gerade das, was die Untersuchungen über das Milzbrand-Contagium so einfach und so sicher macht, nämlich die unverkennbare Form der Bacillen und die durch Impfung fortwährend über sie ausgeübte Controle, würden für Typhus und Cholera fehlen. Trotzdem dürfen wir uns durch die für manche Krankheiten vorläufig noch unüberwindlich erscheinenden Hindernisse nicht abschrecken lassen, dem Ziele, so weit als unsere jetzigen Hilfsmittel es zulassen, nachzustreben. Nur darf man nicht, wie bisher, mit dem Schwierigsten beginnen. Erst muss das Naheliegende erforscht werden, was von unseren Hilfsmitteln noch erreicht werden kann.

Durch die hierbei gewonnenen Resultate und Untersuchungsmethoden müssen wir uns dann den Weg zum Ferneren und Unzugänglicheren zeigen lassen. Das vorläufig Erreichbare auf diesem Gebiete ist die Aetiologie der infectiösen Thierkrankheiten und derjenigen menschlichen Krankheiten, welche, wie Diphtheritis, auf Thiere übertragen werden können. Diese Krankheiten gestatten uns, die für diese Untersuchungen allein nicht mehr ausreichende Kraft des Mikroskops durch das Thier-Experiment zu ergänzen.

Nur mit Zuhülfenahme einer so gewonnenen vergleichenden Aetiologie der Infectiouskrankheiten wird es möglich sein, das Wesen der Seuchen, welche das menschliche Geschlecht so oft und so schwer heimsuchen, zu ergründen und sichere Mittel zu finden, um sie fern halten zu können.

Wollstein, Grossherzogthum Posen, 27. Mai 1876.

FIGUREN-ERKLÄRUNG

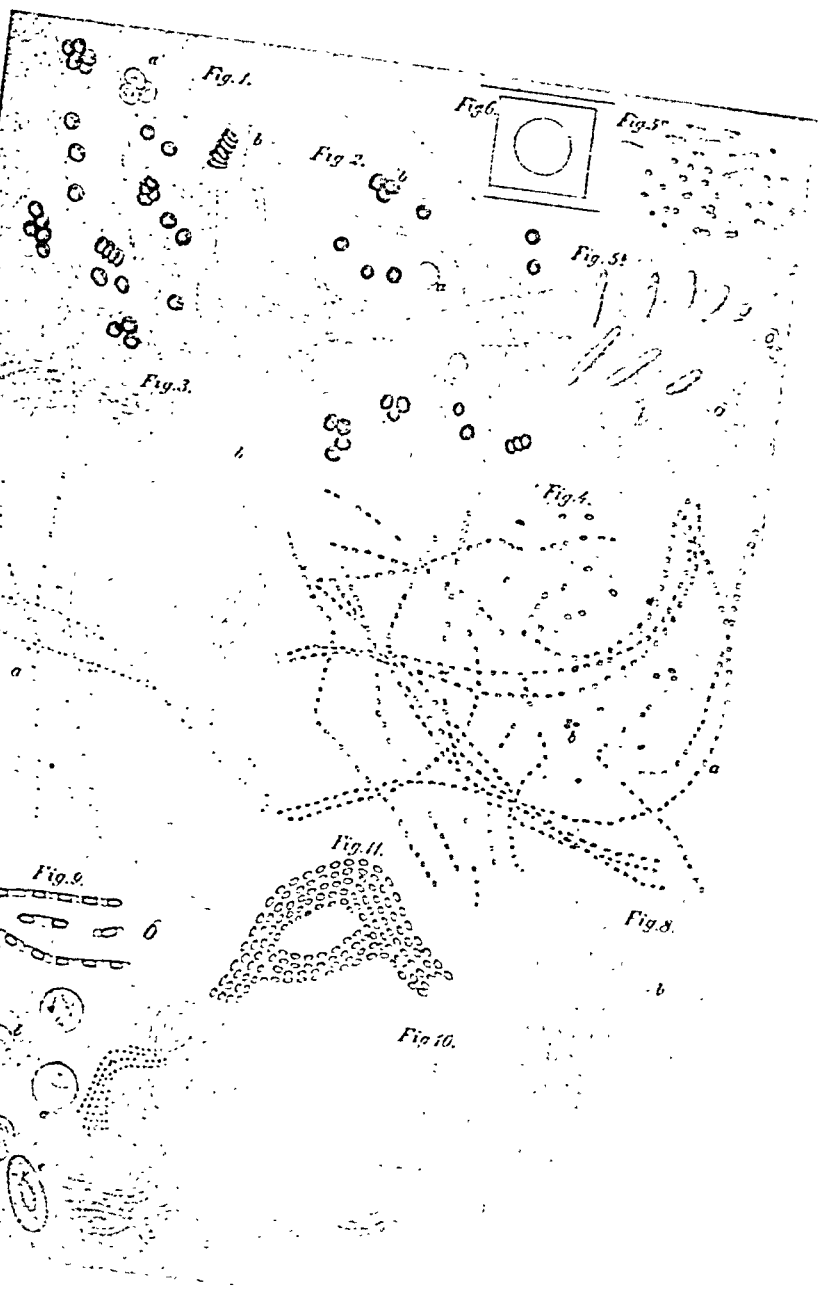
TAFEL XI.

ENTWICKELUNGSGESCHICHTE VON *BACILLUS*

Fig. 1–7 Milzbrandbacillen (*Bacillus Anthracis*)

- Fig. 1. Milzbrandbacillen vom Blut eines Meerschweinchens; die *Bacillen* als glashelle Stäbchen, zum Theil mit beginnender Quertheilung oder geknickt, a weisse, b rothe Blutkörperchen (p. 282).
- Fig. 2. Milzbrandbacillen aus der Milz einer Maus, nach dreistündiger Cultur in einem Tropfen *Humor aqueus*; in Fäden auswachsend, um das 3–8 fache verlängert, zum Theil geknickt und gekrümmt (p. 282).
- Fig. 3. Gesichtsfeld aus dem nämlichen Präparat nach zehnstündiger Cultur; die *Bacillen* in lange Fäden ausgewachsen, die oft zu Bündeln um einander geschlungen sind; a in einzelnen Fäden erscheinen stärker lichtbrechende Körnchen in regelmässigen Abständen (p. 282).
- Fig. 4. Gesichtsfeld aus dem nämlichen Präparat nach 24 stündiger Cultur; a in den Fäden haben sich länglich runde Sporen perl schnurartig in regelmässigen Abständen entwickelt; b manche Fäden sind in Auflösung begriffen, die Sporen frei, einzeln oder in Häufchen zusammengeballt (p. 283).
- Fig. 5. Keimung der Sporen; a mit Hartnack 9 Imm. von Koch, b mit Seibert VIII. Imm. von Cohn gezeichnet (vgl. p. 289). Die Spore verlängert sich in ein walzenförmiges Körperchen, die stark lichtbrechende Masse bleibt an einem Pole liegen, wird kleiner, zerfällt in 2 oder mehr Particen und ist schliesslich ganz verschwunden.
- Fig. 6. Darstellung der Cultur der Milzbrandbacillen in einem hohlgeschliffenen, mit einem Deckglas bedeckten, vermittelst Olivenöl ringsum luftdicht abgeschlossenen und durch einen heizbaren M. Schulze'schen Objecttisch auf Blutwärme erhitzten Objectträger; Natürl. Grösse. Die *Bacillen* befinden sich in einem Tropfen von frischem *Humor aqueus*; schon mit blossen Augen erkennt man die von der Stelle der Aussaat in den Tropfen hineingewucherten, leicht flottirenden äusserst feinen Fadenmassen (p. 284).

Fig. 7. Gesichtsfeld aus der Umhüllungsschicht eines unter die Rückenhaut eines Frosches gebrachten Stückchens von der Milz einer milzbrandigen Maus; die Schicht besteht aus grossen, kernhaltigen Zellen a; in einzelnen Zellen sind mehrere kurze, etwas geknickte oder gekrümmte, zu Haufen vereinigte oder spiralig gedrehte *Bacillen* (b) aufgenommen, welche in den Zellen weiter wachsen und diese zuletzt sprengen; c zusammengefallene Zellmembranen, g freigewordene *Bacillenspiralen*; e Blutkörperchen des Frosches; auch unveränderte *Bacillen* sind sichtbar (p. 301).





Investigations of Bacteria

The Etiology of Anthrax, Based on the Ontogeny
of the Anthrax Bacillus

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INTRODUCTION. Ever since the finding of bacilliform bodies in the blood of animals dead from anthrax great efforts have been made to prove that they are the cause of the direct transmission of this disease and also responsible for its sporadic appearance, and therefore the true contagium of anthrax. Recently, Davaine, particularly, has studied this problem and, supported by numerous experiments with inoculation of fresh and dried blood containing rod-like bodies, has declared with great certainty that these rods are bacteria in the anthrax blood. The direct transmission of developed cases of anthrax in man and animals, although not definitely demonstrable, he attributed, as he had discovered it, to the spreading of bacteria, which remained viable in the dry state for a long time, through air currents, insects and the like. The manner of the spreading of anthrax seemed to be explained fully in this way.

Nevertheless, these statements proposed by Davaine were met with contradiction by various authors. Some investigators claimed to have produced fatal anthrax after inoculation with

bacteria-containing blood, (p. 278) without the later presence of bacteria in the blood and, conversely, that it was possible to produce, by inoculation with this bacteria-free blood, anthrax in which bacteria were present in the blood. Others called attention to the fact, that anthrax does not depend on a contagium which is disseminated above the earth's surface, but that this disease stands in an undoubted relationship with conditions of the soil. How could one otherwise explain that the endemic occurrence of anthrax is associated with a moist soil, namely, in river valleys, swampy districts and lake regions; that, also, the number of anthrax cases is considerably greater in wet years and are massed chiefly into the months of August and September, in which the curve of the heat of the soil reaches its maximum, and that as soon as the herds of cattle are led to certain pastures and drinking places in the anthrax districts, a greater number of affections with this disease appears every time among the animals?

These conditions are certainly not explainable by the assumption of Davaine and the insufficiency has resulted in the complete denial by many people of the importance of the bacteria in anthrax.

As on several occasions I had the opportunity of examining animals that died from anthrax, I utilized these in a series of experiments, which were intended to explain the above mentioned dark points in the etiology of anthrax. In these I very soon came to the conviction, that the Davaine theory of the method of dissemination of anthrax is only partly right.

It appeared that the bacilli of anthrax blood are not as resistant by far as Davaine believed himself forced to conclude. As I will show later, the blood, which contains only bacilli, retains its inoculability in a dry state for only a few weeks and in the moist state for only a few days. How could such easily perishable organisms, slumbering often during the entire winter and in moist soil perhaps for years, form the contagium of anthrax? If the bacteria are actually the cause of the anthrax, there remains nothing else than to assume that as a result of a metagenesis they may be transformed into a state insensitive to alternating desiccation and moistening, or, what is far more probable and has

been indicated by Prof. Cohn, (p. 279) that the bacteria form spores which possess the property of growing anew into bacteria after longer or shorter resting states.

All my further experiments were directed to discovering this suspected developmental state of the anthrax bacillus. After some fruitless endeavors it was possible finally to achieve this goal and thereby to determine the true etiology of anthrax in its characteristic features.

As the ontogenesis of the anthrax bacillus offers not only a botanical interest, but can also throw some light upon the presently undetermined etiology of infectious diseases dependent upon the soil, I have now undertaken, although my experiments are not yet concluded, to publish the most important results of them.

II. Ontogenesis of the Anthrax Bacillus. According to Prof. F. Cohn's classification of the schizophytes,* the anthrax bacilli belong to the species *Bacillus* and have been given the name *Bacillus anthracis*, which I will subsequently use instead of the inclusive term *Bacteria*.

1. In the blood and the tissue juices of the living animal the bacilli multiply extraordinarily rapidly in the same manner as has been observed in various other sorts of bacteria, namely, by elongation and transverse division.

It has by no means been possible for me to see this process directly; however, the same may be concluded from the inoculation experiments frequently done already and repeated by me in the following manner. As a very convenient and easily obtainable subject for inoculation I have usually used mice. At first I inoculated them on the ears or in the middle of the tail, but found this method uncertain, as the animals could remove the inoculated material by rubbing and licking; later I selected as the site of inoculation the back of the root of the tail, where the skin is easily movable and covered with long hairs. For this purpose, the mouse, confined under a large glass, is grasped with a long forceps by the tail and the latter is pulled out through a narrow slit between the cover and the edge of the glass far enough to enable one to make a flat transverse incision into the skin of the

* Beitr. z. Biol. d. Pflanz., 1, No. 3: 202.

back of the root of the tail after which the smallest possible drop-let of the bacillus-containing fluid is applied to the small wound. (p. 280) Inoculations carried out in this way, which I have made in great numbers, have had without exception a positive result, provided very fresh anthrax substances have been used; and I believe, therefore, that I can consider such an inoculation as a certain test of the life or death of the bacilli, according to the result; a view, which has been proved to be correct by other experiments to be mentioned later.

Partly, then, in order to be supplied with fresh material, and partly also to prove whether after a definite number of generations the bacilli undergo transition into another form, mice were inoculated several times in successive series, so that without interruption the succeeding mouse was always infected with the spleen substance of the one that died shortly before from anthrax. The longest of this series consisted of twenty mice, so that there were just so many generations of the bacilli; the spleen was always considerably swollen and filled with innumerable amounts of hyaline rods, which showed slight differences in size, were immobile, and showed no spore formation or the like. These bacilli were also present in the blood, but were by no means as numerous as in the spleen. In these experiments there repeatedly developed from a few bacilli, as a result of many generations, considerable masses of similarly formed individuals of the sort one sees among newly developed bacilli. There were many with a beginning transverse division in the middle, some with a kinking at this site, and still others hanging together at an angle, and so another method of their multiplication than by elongation and transverse division, after they have reached about double their length, can hardly be assumed. According to this result, it could scarcely be expected that a change in the form of the bacilli could be achieved by a still longer series of inoculations, or that a different kind of generation could be found. And at the site of inoculation of the adjacent seriously infiltrated hypodermic cellular tissue and in the adjacent lymph nodes only short bacilli and those in the act of division were found in rabbits and guinea-pigs.

The distribution of the bacilli in the body of the inoculated animals is not always uniform. In the guinea-pig the blood contained extraordinarily many bacilli, so that their number often equalled or even exceeded that of the erythrocytes; in the blood (p. 281) of the rabbit they were considerably less numerous, often so rare that several microscopic fields had to be examined before a few were found; in mice the blood always contains such a small number of bacilli that they sometimes seem to be entirely absent.* On the other hand, one finds the bacilli all the more abundant and the more certainly in the lymph nodes and the spleen in rabbits, and in mice surprising amounts in the spleen. A few times I have examined the marrow substance of the tibia of mice, but found only isolated bacilli in it.

The other associated details as to the deposition of the bacilli in the tissue of the spleen, in blood vessels, as to their accumulation in the capillaries and small veins and the resulting local edemas, vascular ruptures and escape of blood, I do not wish to enter upon because of the purely pathologic interest of these conditions.

It would also lead me too far to discuss the question of the true cause of death of animals dying from anthrax, and whether these are killed by the carbonic acid developed by the intensive growth of the bacilli in the blood or, what is more likely, by toxic albuminous bodies consumed by the parasites for their nourishment.

2. In the blood of the dead animal or in other suitable nutrient fluids the bacilli grow within certain limits of temperature and in the presence of air to extraordinarily long, unbranched, leptothrix-like threads, with the formation of numerous spores.

One is convinced most easily of the correctness of this statement by the following experiment:

A drop of cattle blood serum (as fresh as possible) or of the aqueous humor of cattle eye is placed on a slide; in this a small

* Such cases, when only the blood of animals inoculated with anthrax was examined, probably led to the previously mentioned view, that the anthrax occurs without the presence of bacilli in the blood, and that one can again produce anthrax by inoculation with bacillus-free blood.

piece of fresh bacillus-containing splenic substance is dropped and the cover glass is applied over this in such a way, that the bacillary mass comes to lie in the centre of the specimen. In order to avoid drying the fluid, the slide is immediately placed in a moist chamber and with this into the incubator.*

(p. 282) The water content of the air in the moist chamber must be so regulated that the fluid does not escape from under the cover glass and the serum does not dry at the edge of the cover glass. In the former case, the bacilli under the cover glass are washed away and escape observation, while in the latter the dry layer of serum walls off the air from the bacilli and any further development is thereby prevented.

The specimens prepared in this way remain in the incubator for 15 to 20 hours at a temperature of 35 to 37 degrees C. In an examination undertaken at that time, there are in the centre of the specimen (Plate XI, Fig. 1) between the still intact cells of the splenic pulp and the erythrocytes many unchanged bacilli, but in a smaller number than in the fresh specimen. But as soon as one leaves the centre of the specimen, one finds bacilli that are elongated three to eight times their original length and at the same times show some slight kinks and flexures (Fig. 2). The nearer one approaches the edge of the cover glass, the longer are the threads; these show many torsions and finally reach a hundred and more times the length of the original bacilli (Fig. 3). Many of these long threads have lost their uniform structure and transparency; their content is finely granular and in places there appear small, more refractive granules at regular distances (Fig. 3a). Lying close to the edge, in the threads which are located most favorably in regard to the interchange of gases in

* For the moist chambers I used flat plates filled with wet sand; a layer of filter paper lay on the sand, and on this the specimen. The plate was covered with a glass plate. When the layer of sand is so deep that the distance between the surface of the specimens and the inferior surface of the glass plate is 0.5 to 1.0 cm., the specimens remain sufficiently moist. To all who would undertake such experiments with the incubator without gas or a regulator, I cannot highly enough recommend this method of heating. As one can heat a large apparatus with a small flame, with a moderately large kerosene reservoir in the lamp it is necessary only to fill the lamp about once daily and to test the height of the flame at the proper level for the desired temperature, in order to have a constant temperature varying between 1 to 2 degrees without special care or supervision.

the nutrient fluid, the development has progressed the most. These threads contain fully developed spores, which are deposited in the form of somewhat elongated, round, (p. 283) markedly refractive bodies at very regularly short distances in the substance of the threads (Fig. 4a). In this form, especially when they are much intertwined and grouped in lines winding around one another, the threads make a surprising picture, which may best be compared with that of the most delicate and artificially arranged string of pearls.

Some of the threads are already involved in the process of dissolution and their former form is still indicated only by the link-formed position of the spores held together by a mucous connecting substance. Between them there occasionally lie isolated free spores and spores conglomerated into small heaps (Fig. 4b). In such an isolated well-prepared specimen all the transitions from the short bacillary rods up to the long spore-bearing threads and free spores are present and with it can be brought proof that the latter have originated from the former. In spite of the fact that I originally repeated this experiment several times and always obtained the same result, various doubts as to the correctness of this assumption arose in my mind. How did the bacilli, in which I heretofore observed no independent motion, come to the edge of the specimen, while the erythrocytes remained in the centre? Could not the long spore-bearing threads possibly have developed at the edge of the fluid through germs having reached there from the air? For the specimens were not protected against such a contamination from the air and, in fact, the prettiest colonies of *Micrococcus* and *Bacterium* often proliferated in this way next to the threads in the specimen; a few times there also appeared a type of bacillus similar to ours. All depended, therefore, upon absolute certainty and upon not falling into an error. Unfortunately in the past, such an error has frequently been made by experienced investigators in experiments of culturing the lowest form of organisms. As a result of these errors, investigations in this field have in recent times come to be somewhat discredited. I refer to the mistake of immediately pronouncing similar forms, which develop simultaneously or

shortly after each other in the same nutrient fluid and intermingle with apparent transitional forms, as different developmental stages of the same organism.

Inasmuch as the conditions for the development of the *Bacillus anthracis* were known to me, namely, the nutrient fluid, the temperature at which it grows and the necessity for the access of air, I endeavored to provide these demands on the microscope table, (p. 284) in order to be able to observe the change of the bacilli directly.

As difficult as at first I imagined this experiment to be, so simple it proved in reality. After many a fruitless experiment I found the following method to be most useful:

As the source of heat I used M. Schulze's heatable stage for examining objects, which I heated with a kerosene lamp just as was previously described with the incubator. The microscope must be placed on a support in order to bring the lamp, which is supplied with a flat kerosene reservoir made of tin, with its chimney under the arm of the heatable stage. A single small flame, standing about under the centre of the one arm, sufficed in my apparatus to maintain the stage for days at the necessary temperature. The moist, air-containing chamber was replaced by a hollow ground glass slide covered by a cover glass. The amount of air supplied in this way to the bacilli for their development is very slight, but as experience teaches, sufficient for the success of the experiment. In order to find the proper temperature for the hollow ground glass slides of the sort used by me, I utilized the melting point of cattle tallow, which was estimated in the water bath fairly accurately at 40°C . A droplet of this previously-tested cattle tallow was placed on a glass slide and this slide in turn was placed in the cavity of the hollow slide with the tallow droplet directed downward; the cavity was made airtight by a layer of Provencal oil painted all around it. It was found that the stage had to be heated to 45°C . in order to bring the drop under the cover glass to the melting point. For the temperature necessary for my experiments it was sufficient to heat the stage to such a degree that its thermometer constantly pointed to 40°C . At the same time it became noticeable that the approach of the

tube of the microscope, as is necessary for adjustment of an object with a Hartnack objective lens 7 and an ocular 3, which I used in these experiments, had a markedly cooling effect each time and reduced the temperature in the drop by 5 to 8 degrees. After these findings I placed a drop of fresh cattle blood serum or, what proved better for this experiment, a drop of fresh and pure aqueous humor of cattle eyes, on the under surface of the cover glass. Naturally, the drop must not be too thick (p. 285) that all its layers may not be seen with the microscope.* The smallest possible amount of fresh bacillus-containing splenic substance was then introduced at the edge of the drop and the cover glass was immediately placed onto the glass slide painted with the oil. The small cavity rapidly filled with steam and the initial evaporation of the drop was so slight, that a few bacilli dried up only at the outermost edge; later the drop maintained its form intact for days. The specimen prepared in this way was then placed on the warm stage and after the currents in the warming fluid had subsided, and some of the bacilli lying more toward the centre of the drop had become fixed and had been drawn quickly according to their form and position, the tube of the microscope was screwed up in order to avoid an asymmetrical and too prolonged cooling of the specimen. At the following examinations made every ten to twenty minutes, it was seen that the bacilli at first became somewhat thicker and apparently swelled up, but hardly changed during the first two hours. Then their growth began. After three to four hours they had reached ten to twenty times their former length, they began to bend, and to displace one another or to move among themselves as in a network. After

* Among the different types of hollow ground glass slides I found the most convenient to be one 3 mm. thick which, incidentally, is 60 mm. long and 20 mm. wide. Its upper surface is ground lusterless; the cavity has the form of a spherical section, a diameter of 14 mm., and a depth of 1.5 mm. Hartnack's cover glasses, 18 mm. square and 0.15 mm. thick, may very well be fastened air tight on such slides with oil. The drop on the under surface of the cover glass I gave a diameter of about 5 to 7 mm., so that it remains about 3 to 5 mm. removed from the oil all around and even when the oil flows somewhat inward under the cover glass, cannot easily reach it. In the culture experiments in the incubator, I have found glass slides with a paraffin ring very practical. One can easily make them in every desired size and form and use them in exactly the same way as hollow ground glass slides.

a few additional hours, the individual threads were already so long that they covered several microscopic fields; they simulated a heap of glass threads which unite in the manner of creeping plants in the most varying manner, sometimes in long parallel files or in extremely delicate spirally formed twisted bundles, and sometimes in the most irregular figures of an inextricable tangle. (p. 286) It was absolutely impossible to follow the individual thread for its entire length.

If one observes the free end of a thread continuously for a long time, after about 15 to 20 minutes it is easy to see a continuous elongation. One can get an idea of the remarkable play of visible growth of the bacilli and can obtain immediate proof of its further development. After 10 to 15 hours the content of the strongest and most luxuriantly grown threads appear finely granular and very small, pale, glistening granules are soon given off. These enlarge after several hours into the markedly refracting egg-round spores. Gradually the threads then degenerate and crumble at their ends. The spores become free, sink to the lower layers of the drop according to the laws of gravity, and accumulate there in dense heaps. The specimen then remains in this state unchanged for weeks. The illustrations on Plate XI (Figs. 1-4) give the truest possible picture of the various stages of development of the *Bacillus anthracis* described above.

Occasionally various kinds of bacteria appeared in large swarms and resting colonies as unwelcome guests even in the specimens that were prepared and treated in this manner, and disturbed the observation of the later developmental stages of the *Bacillus anthracis*. When one prepares a great number of specimens with some care, using fresh, pure aqueous humor or blood serum, and immediately places the splenic substance taken from the dead animal in the incubator, one finds on repeated examinations in at least half, more often in all the specimens, an absolutely pure culture of anthrax bacilli. If under the conditions mentioned above the development of the bacilli does not occur at all, or if they grow poorly and spore formation does not occur, there is some error in the preparation of the experiment. One of the trivialities that may be responsible for poor development can be seen

from the following experience. At first some of my cultures failed to grow because I placed all the cover glasses after their use into a solution of carbolic acid. In spite of careful cleaning, traces of carbolic acid, recognizable by smell, occasionally persisted on the cover glasses. Only after I had convinced myself by control experiments that such extremely slight (p. 287) amounts of carbolic acid are sufficient to disturb the culture of the bacilli and I had, accordingly, thoroughly cleaned the cover glasses by repeated flushing, was I spared these failures. At one time I was absolutely unable to bring the threads to spore formation; they grew in peculiar curling, fairly large forms, but finally degenerated. Afterward they grew only isolated spores or no spores at all. In vain I searched for the cause in a faulty construction of the heating apparatus, in the nutrient fluid, or in other factors. Finally it occurred to me that the oil used for the sealing of the specimen smelled of volatile oils. I then prepared several specimens at the same time in exactly the same manner, but used a rancid oil for some and a perfect Provencal oil for the fastening of the cover glass of others. The bacilli in the latter specimen showed the most perfect spore formation but in the former the spores appeared only sparsely. As this effect of the volatile fatty acids, or perhaps of only a certain acid, which did not come into direct contact with the drop containing the bacilli but could only act upon it by a very slight amount of their gases, seemed very remarkable, I repeated this experiment at different times and always obtained the same result.

3. The spores of the *Bacillus anthracis* develop under certain conditions (a definite temperature, nutrient fluid and access of air) immediately from bacilli originally occurring in the blood. That the shiny bodies formed in the long threads are in fact spores and not some accidental products of degeneration or residua of the degenerating bacilli can be assumed with certainty by the analogy of the ontogenesis of other organisms in the series of fungi and algae. Inoculation experiments to be mentioned later with fluids which although containing only spores of *Bacillus anthracis* and no traces of bacilli or threads were yet able to produce anthrax with the same certainty as those containing

fresh bacilli, confirmed this assumption. But in order to gain a complete insight into the course of life of the *Bacillus anthracis*, the wisest procedure was to continue the path formerly followed. It was important to learn in what manner the spores again underwent transition into bacilli, whether directly or indirectly as a zoöspore living in water. (p. 288) If possible, a way had to be found to allow the germination of the spores under conditions which afforded a direct microscopical observation.

All efforts at producing the further development of the spores in distilled water and well water at an ordinary temperature or at 35°C. failed. Cultures attempted in blood serum or aqueous humor, according to the methods described above, in closed cells and in the incubator led to incomplete results; there developed undoubted bacilli, which grew into long threads and developed spores; but their number was small and the transition of isolated spores in the bacilli could not be followed in the heaps of spores with definite certainty. Finally, I used the following procedure which led to the goal. Droplets with masses of spores taken from specimens, which after microscopical testing contained a pure culture of *Bacillus anthracis* and after the long threads were completely or mostly degenerated, were placed on a cover glass. These were too rapidly dried, partly close to the edge and partly toward the centre of the cover glass. This drying kept the heaps of spores together and did not allow them to be washed away and separated by the nutrient fluid. The masses of spores remained dry for several hours or even days; then a drop of aqueous humor corresponding to the size of the cover glass was placed on an ordinary glass slide (not hollow ground) and the cover glass was laid on it in such a way that the masses of spores were moistened by the fluid. This specimen, which was sealed with oil, was placed in the previously described moist chamber and with this in the incubator, which was heated to 35 degrees C.

After a half hour, the residua of the fully grown threads, still lying here and there between the spores, began to degenerate completely and after about one and one-half to two hours they had disappeared.

After three to four hours a development of the spores was already noticeable.

This development of the spores progressed most rapidly in the heaps at the edge of the cover glass; they had already almost completely changed into threads, while toward the centre of the specimen all transitions from these threads into simple spores were found. Following observations on many such specimens the development of the spores was seen to occur in the following manner:

(p. 289) On careful examination with greater magnifications (for example, Hartnack immersion 9) every spore appeared in an egg-shaped form embedded in a spherical, transparent mass which looked like a bright, narrow ring surrounding the spores. The spherical form was easily recognized when the spore rolled in different directions. The mass first lost its spherical form, became elongated in the direction of the long axis of the spores toward one side, and became longitudinally egg-shaped. At the same time the spore remained lying in one pole of the small cylindrical body. Very soon the transparent covering became longer and thread-shaped and at the same time the spore began to lose its strong luster. It rapidly became paler and smaller and was broken up into several parts, until it finally disappeared entirely. Such a heap of spores with the transitions into threads is illustrated in Figure 5.

Later I was often successful in growing the spores from the bacilli in the same specimen and in the same drop of aqueous humor, and immediately from these again a second generation of spore-bearing threads. If only a few bacilli reached into the drop, the spore formation was completed, as usual, after about twenty to twenty-four hours, the nutrient material, however, was not yet exhausted and a few hours later the spores again grew into bacilli, and these into threads.

Especially in such specimens could the transition of the spores into the bacilli be observed with certainty; Figure 5b was taken from such a specimen and Prof. F. Cohn was kind enough to prepare this drawing himself with the use of magnification with a Seibert immersion lens VIII. From these simple changes in the

form of the spore during its germination it is evident that it consists of a markedly refractive droplet, perhaps of an oil which is surrounded by a thin protoplasmic layer. The latter is the true developing cell substance, while the former constitutes perhaps a reserve substance utilized in the germination.

With this last series of investigations the circle formed by the changes in the form of the *Bacillus anthracis* is closed and there is given the complete ontogenesis of this bacillus.

In recent years the most wonderful observations and the most contradictory views on pathogenic schizophytes have often been published. Therefore, as I have indicated before (p. 290), works of this sort have been received both by botanists and physicians with a well justified distrust. Accordingly I again call particular attention to the fact that my investigations are not based upon accidental or isolated observations, but always on experiments repeated as often as possible and with absolutely definite results.

In order to give every one who is interested in this subject an opportunity of convincing himself without difficulty by seeing the correctness of the results of my investigation, I have described as accurately as possible the methods, acquired by difficult and time-consuming experiments, according to which I have worked. I also lay great importance on the fact, that at my request Prof. F. Cohn, to whom I owe special thanks for his trouble, tested and in every respect confirmed my statements regarding the ontogenesis of the *Bacillus anthracis* in a series of specimens and experiments at the Pflanzenphysiologischen Institut in Breslau.

The literature on the anthrax bacillus has been available to me only in part and I, therefore, must abstain from a complete bibliography. I would like to mention briefly a few works which I became acquainted with after the discovery of the ontogenesis of the *Bacillus anthracis*. Bollinger* thinks that bacilli are made up of rows of spherical bacteria, to which they occasionally degenerate, and that these spherical bacteria occur only in the blood, multiply by division and, reunited in rows, may again form rods. Accordingly, it might almost appear as if Bollinger had also seen

* Ziemssen's Handb. der spec. Pathol. und Therap., 3: 464.

the spore formation. But this is not the case, as he reports to have seen only once bacilli of 0.05 mm. length, a size at which the bacilli do not undergo spore formation.

In the discussion of Bollinger's views mentioned above, F. Cohn states that he considers the anthrax rods to be bacilli and that by analogy of other bacilli a propagation of them by spherical permanent spores must be expected. (p. 291) This suspicion soon became verified. The most recent publication on anthrax bacteria by C. O. Harz, according to the reference available to me (Allgem. med. Centralzeitung 1876, No. 33) contains only negative results, which must lose their importance when compared with my positive findings.

III. The Biology of the Anthrax Bacillus. The possibility of developing the *Bacillus anthracis* into spore-bearing threads under artificial conditions and these spores again into bacilli naturally does not prove that occurrence of anthrax under all conditions must be traced to the different developmental forms of this type of bacteria. As it does not develop further in the living organism, as has already been shown (at present conclusively only for the animal species, with which experiments have been done), an explanation thereof can be sought only by experiments on the behavior of the *Bacillus anthracis* under conditions to which it is ordinarily subjected after the death of the animal infested by it.

Not to go too much into details, I must briefly review the very extensive series of experiments conducted along these lines.

Substances which contain anthrax bacilli may be disseminated in the dry state or suspended in fluids. It has been known that they may be active for a long time in the dry state; however, the reports on the duration of this activity vary. The following experiments were carried out in order to determine the latter more accurately:

Spleen, lymph nodes, and the blood of mice, rabbits and guinea-pigs, immediately after being removed from the body, were dried in a shady and airy place, in larger pieces, in smaller masses from about the size of a pea to that of a millet seed, and in thin layers dried on a cover glass. One or more mice were inoculated and a

culture experiment was conducted in a paraffin cell with this material, at first daily, later every two days after a corresponding amount was softened in aqueous humor. The bacillary masses dried in very thin layers, according to their thickness, lost their inoculability after 12 to 30 hours and also the possibility of growing into long threads in the incubator. Immediately after moistening them the bacilli had the same appearance as in the fresh state, but they very soon degenerated under conditions to be described more fully later; (p. 292) after they had lost a certain portion of their moisture, they died. Thicker dried pieces retained their inoculability and power of development for two to three weeks. Still larger pieces retained their effectiveness for about four to five weeks, apparently because they dried more slowly. But I have never been able to keep freshly dried bacillary masses inoculable for a longer time, although I have modified and repeated these experiments in various ways. This is because I depended upon Davaine's statements and definitely believed that I could secure freshly maintained anthrax substances for later experiments; but I was most sadly mistaken and therefore had to interrupt my work several times, until I finally succeeded in securing a constantly effective inoculation material in another way and thereby made myself independent of any accident.

I must call special attention to a phenomenon which appeared very striking in this series of experiments, namely, that only those dried substances which developed spore-bearing threads in the culture experiments would produce anthrax, and vice versa. This observation alone would be sufficient to prove that the transmissibility of anthrax is dependent upon the presence of viable bacilli.

Before I proceed to the experiments on anthrax fluids, I must mention a series of culture experiments at different temperatures. I was chiefly interested in finding the lowermost limit of temperature at which the *Bacillus anthracis* was still able to develop spores capable of germinating. A number of paraffin cells were implanted, in the manner previously described, with nutrient fluid and fresh viable bacilli and then preserved at different temperatures. As this experiment was conducted during the winter,

it was easy for me to keep individual specimens cooled down to 5 degrees C. The higher temperatures (over 40 degrees C.) were maintained with the heatable stage. In this way it was found that the threads grow most rapidly at 35 degrees C.; even after twenty hours at this temperature they may be supplied with the most beautiful spores. At 30 degrees C. the spores appear somewhat later, namely, after about thirty hours. With a still lower temperature the development of the bacilli also becomes correspondingly slower. At 18 to 20 degrees (p. 293) (Cels.), namely, the normal room temperature, they require about two and a half to three days for the development of spores. Below 18 degrees spore formation occurs only exceptionally, and under 12 degrees no growth of the threads is observed at all. Below 40 degrees C. the development of bacilli is poor and seemed to me to cease at 45 degrees; however, I have not repeated the experiments with the growth of the bacilli at the upper limits of temperature often enough to be able to report on them very accurately (as the heatable stage allows the observation of only a single specimen).

I now come to the subject so extremely important in the etiology of anthrax, namely, the behavior of the bacilli in different fluids and under natural conditions. Because a very small amount of blood was obtainable from the experimental animal available to me, the mouse, and because this blood contained very small amounts of bacilli, I used fresh cattle blood or aqueous humor and a few times also vitreous bodies from cattle eyes. I rubbed up fresh mouse spleen containing bacilli into these fluids, until the amounts in the mixture approximately equalled the blood, serous and mucous fluids of animals dead from anthrax.

Such fluids poured into a well corked glass very rapidly take on a most penetrating putrefactive odor in the incubator. The bacilli disappear after twenty-four hours without growing any threads and it is then no longer possible to produce anthrax with them. That the death of the bacilli in this case depends less upon the influence of the developing putrefactive gases, which cannot escape, than upon the lack of oxygen can easily be shown by the following experiment. A drop of blood containing bacilli is placed between an ordinary glass slide and a cover glass without

air bubbles, is made air tight by a layer of oil painted around the edge and is warmed on the heatable stage. When examined under the microspectroscope, the blood shows the two bands of oxyhemoglobin; at this time the bacilli, just as in the cell specimens, begin to elongate and after about three hours reach four to five times their original length. The oxygen is then exhausted, the two bands disappear and between these bands one band of reduced hemoglobin appears. From this time forward the further growth of the bacilli also completely ceases, although (p. 294) no putrefactive bacteria can be seen as yet and the true putrefaction has not yet begun.* In such a specimen, if it is kept at a low temperature, one can in an excellent manner study the changes in the bacilli in the process of dying. This process occurs in the following manner. Fresh bacilli and those engaged in lusty growth (excepting at the time just before the formation of spores) always have a homogeneous transparent content and show only very isolated articulation, indicated by angular kinks. The first sign to be recognized in the bacilli is a clouding of the content and a severance into shorter divisions. The bacilli then appear more or less distinctly articulated as the extremely fine cell membrane surrounds and holds together these parts as in a sheath. But very soon the bacilli lose their sharp contours and seem to consist of short, circular pieces hanging loosely together. They finally degenerate completely. From time to time, often for days, I have observed isolated bacilli degenerated in this manner in the most varying kinds of specimens, but have never seen a transition of the same into micrococci or the like.

On the other hand, entirely different pictures are obtained on repeated examinations of the bacillus-containing fluids mentioned, when access of oxygen is made possible, even though it is in very small amounts, and the temperature is not reduced permanently below 18 degrees C. The resulting changes can be followed very well, if about 10 to 20 gm. of the fluid in a watch

* In the unopened body of an animal dead from anthrax the bacilli elongate, but when the cadaver is left for a long time at a temperature of 18 to 20 degrees C. they elongate very slightly or not at all; apparently this occurs because the oxygen of the blood after death is rapidly exhausted by oxidative processes and is not restored again.

crystal, upon which a loosely occluding glass plate is placed, remain for several days at room temperature. After twenty-four hours the fluid takes on a putrefactive odor, which is usually very penetrating after an additional twenty-four hours. Accordingly, micrococci and bacteria are soon present in large amounts. At the same time the *Bacillus anthracis* flourishes very well, as if it were the only inhabitant of the nutrient fluid. Its threads achieve a considerable length after twenty-four hours; (p. 295) often after forty-eight hours, and even earlier, they have grown spores in large amounts.* After the development of the spores the threads degenerate and the spores sink to the floor. The vegetation of the other schizophytes, which at times accidentally penetrated the fluid and multiplied therein, proceeds for days in the most luxurious manner. But gradually these also disappear, the characteristic odor of putrefaction diminishes, a muddy deposit finally forms and the supernatant fluid becomes poor in formed elements and almost clear. It finally has a weak odor of lime or cheese and no longer undergoes any change if it is protected from drying by the addition occasionally of distilled water; the putrefactive process is completed.

When substances containing bacilli are moderately diluted with distilled or well water, the formation of spores is not prevented; but with greater dilution the bacilli no longer develop,† but soon die and after thirty hours' incubation no longer produce anthrax. Therefore, the nutrient fluid must contain a certain amount of salts and albumin (to be calculated more accurately) so that the bacilli can develop spore formation.

There is no doubt that most of the cadavers of animals dead from anthrax that were buried moderately deep during the summer, or lie on the field, in the stable, and in flaying houses, as well as the bloody and bacillus-bearing excreta of the diseased animals in moist soil or in stable dung, afford at least equally as favorable conditions for the formation of spores of the *Bacillus anthracis*,

* Bacilli cultured in paraffin cells at the same time and under the same conditions grew more slowly and more sparsely, possibly because of the considerably diminished supply of oxygen.

† For example, bacilli in mouse spleen diluted with twenty times the amount of distilled water do not grow.

as is the case in the series of experiments described previously. Through these experiments, therefore, proof was offered that the spores of the *Bacillus anthracis* develop not only as a result of artificial culture in exceptional cases, but that this parasite deposits its ovules in innumerable amounts every summer in the soil, the moisture of which prevents the drying of the cavities of the diseased animals while still living, or the nutrient fluids escaping from those already dead from anthrax.

We have already seen that these ovules do not change in water, but again (p. 296) grow into bacilli in aqueous humor and blood serum. It could be assumed from the very beginning that if one or more of these spores in any way reaches the blood stream of an animal susceptible to anthrax, a new generation of bacilli is produced. In order to prove this assumption the following experiments were carried out.

Of two covered watch crystals filled with bacillus-containing blood serum, one was kept in a room and the other was preserved in a cold space at 8 degrees C. From both crystals two animals were inoculated daily. In the blood serum that was kept cold, the bacilli became granular and articulated on the third day. Up to that time it was effective but animals inoculated with it later remained healthy. The inoculations with the blood serum that was kept warm were effective both before and after the spore formations in the threads of the *Bacillus anthracis*; even after fourteen days it was still possible to produce anthrax with such putrescent blood, which contained spores of the bacilli, with the same certainty as with fresh rod-containing spleen. The spores seemed to be able to maintain themselves capable of germination for a very long time in putrescent fluids just as in nonputrescent material. For with vitreous bodies of cattle eyes, in which bacilli from a mouse spleen were allowed to come to spore formation at about 20 degrees C. and which had fully completed their putrefaction after three weeks, anthrax could still be produced by inoculation with absolute certainty even after eleven weeks. The sediment of this fluid with completed putrefaction contained many spores of bacilli held together by small mucous flakes, whereas on microscopical examination of the almost clear fluid several fields had to

be searched before a single isolated spore was found. Naturally, not the slightest trace of threads could be found any longer. From these inoculations with the sediment rich in spores and from those with the fluid poor in spores emanated the interesting fact that mice inoculated with the former material containing many spores died after twenty-four hours, and that mice inoculated with the latter containing less spores died after three to four days. I also especially call attention to the fact that I have repeated this experiment several times and always with the same result.

Flakes containing spores from the same fluid were preserved in an open test tube filled with well water; nevertheless these remained effective in inoculations conducted with them.

(p. 297) The same spore-containing substances were dried. After some time they were again softened with water and subjected to the same procedure. They did not lose their ability to produce anthrax as a result of the drying.

It thus becomes easily explainable why the opinions of investigators regarding the effectiveness of dried anthrax blood vary so widely; one used fresh, rapidly dried blood, which contained no spores and which, as I have shown previously, remains effective at the most for five weeks. Others, on the contrary, performed the inoculation with blood that was dried slowly at room or summer temperature and in which spores had developed. I have a small collection of anthrax substances which were dried under the most varying conditions and at different times and preserved in uncorked, narrow-necked glasses. When my attention was drawn to the importance of spores in dried anthrax masses, I again carefully examined these pieces of dried blood, spleen, and lymph nodes, softened with aqueous humor in glass cells, and noted the characteristic spore-bearing threads of the *Bacillus anthracis*, and their ability to produce anthrax on inoculation. It thus became evident that the parts dried rapidly in small pieces contained no spores and were able to develop neither threads nor spores. Sheep spleen, however, which was dried slowly in larger pieces in a room, and some blood tests, which were conducted with larger amounts and had required several days for

complete drying, contained numerous more-or-less free spores and broken pieces of spore-bearing threads. All of these spore-containing substances produced anthrax after inoculation and often developed the most beautiful spore-bearing threads of the *Bacillus anthracis* in the nutrient fluid. The length of time that the dried spores will remain capable of germination cannot be definitely stated at this time; this duration of time will probably include a rather long number of years; at any rate, only recently I have many times carried out inoculations which, without exception, produced fatal anthrax with sheep blood that was dried almost four years ago.*

The identity of the disease produced by inoculation with anthrax blood and of septicemia, as well as the (p. 293) converse relationship, has been claimed many times. In order to meet this objection, which could possibly also be applied to my inoculation experiments made with putrescent anthrax substances, I have several times inoculated mice with putrescent blood of healthy animals, with bacillus-free putrescent aqueous humor, and with vitreous humor of mice. These almost always remained healthy, and only two of the twelve inoculated died a few days after the inoculation; they had an enlarged spleen, but this, as well as the blood, was entirely free from bacilli. In addition, animals were inoculated with putrescent vitreous bodies, in which a type of bacillus very similar to the *Bacillus anthracis* had developed spontaneously. The spores of the two types of bacillus could not be distinguished from each other either by size or by other appearances; only the threads of the vitreous body bacillus were shorter and distinctly articulated. All the inoculations with the bacilli which I found several times in the vitreous body with their spores could not produce any anthrax. Even those animals that were inoculated with spores cultured from bacilli in hay infusion by Prof. F. Cohn, remained healthy. On the other hand, I have several times inoculated masses of spores which were cultured in glass cells and, as I have convinced myself before

* Cases of human anthrax which develop from the handling of hides, hairs, and the like, when these articles have been dried for years, can be produced only by spore-bearing dust particles.

by microscopical examinations, originated from pure cultures of the *Bacillus anthracis*. Every time the inoculated animal died of anthrax. It follows, therefore, that only one type of bacillus is able to produce this specific disease process. Other schizophytes cannot produce this disease and cannot in any other manner act as a disease excitant by inoculation. It might appear as surprising that of my experimental animals inoculated with putrescent blood only occasionally did one die of septicemia. To this I reply, that I did not inject the putrescent blood according to centimeters, as is the usual custom, but I inoculated only an infinitesimal amount of the same into the body of the animal, and in this way, naturally, the probability of introducing the septically acting formed elements present in the blood in perhaps sparse amount, is very much diminished.

That the spores of the *Bacillus anthracis* produce anthrax when they are introduced directly into the lymph stream of the animal body is sufficiently proved by the above mentioned experiments. The spores must, therefore, become effective when they reach wounds either in the dry state as dust particles or suspended in fluids, no matter how small the wounds are. One can hardly find any of our domestic animals, the skin (p. 299) of which is not affected by some scratch wounds or excoriation of the skin produced by chafing, rubbing and the like, and thereby these afford easy access to the dangerous parasite. Nevertheless, this does not imply that the anthrax spores can penetrate the body only in this way. In order to consider the etiology of anthrax completely, the digestive tract and the respiratory organs must also be investigated as to their power of resorption for anthrax bacilli and their spores.

In order to see whether the anthrax contagium can penetrate the body from the digestive tract, I first fed mice for several days with fresh spleen from rabbits and sheep, which had died from anthrax. Mice are extremely voracious and in short time take more than their body weight of masses of anthrax material, so that a very considerable amount of bacilli passed through the stomach and intestines of the experimental animals. But it was impossible for me to infect them in this way. I then mixed

spore-containing fluid in the food of these animals; even this they ate without any harm; no anthrax could be produced in them even with the feeding of larger amounts of spore-bearing blood dried a very short time previously or years before. Rabbits that were fed spore-containing masses at various times also remained healthy. Accordingly, an infection from the intestinal canal does not seem possible in these two species of animals.

Up to the present time I cannot say anything in regard to the behavior of spores reaching the respiratory organs with dust, as it has not been possible for me to conduct experiments on this subject.

I also add a few series of experiments and observations, which have no direct relationship with the etiology of anthrax, but are still interesting enough to be reported.

The experiment made by Brauell, of inoculation with both the bacillus-containing blood of pregnant animals and with the bacillus-free blood of the fetus, I have repeated on a pregnant guinea-pig and two pregnant mice. The result was the same as in Brauell's experiment; the animals inoculated with the maternal blood died from anthrax, while those inoculated with fetal blood remained healthy. In order to see how soon after the inoculation the first bacilli can be found in the blood or in the spleen of the inoculated animal, nine mice were inoculated at the same time. After two, four, six, eight, ten, twelve, (p. 300) fourteen and sixteen hours, one of these mice was killed each time with chloroform and the blood as well as the spleen were immediately examined. No bacilli were found in the first six animals. Only in the mouse killed fourteen hours after the inoculation were isolated bacilli found in the spleen. In the mouse which had lived sixteen hours more bacilli were found and the spleen was enlarged. The last mouse died after seventeen hours with the usual characteristic symptoms; its spleen was considerably enlarged and completely filled with dense masses of bacilli. The penetration of the bacilli into the blood stream, therefore, seems to progress slowly, but after they have once reached there and have gained a firm footing in their true home, they multiply in the most luxurious manner.

Besides the mice, I have also conducted experiments on rabbits

and guinea-pigs, two dogs, one partridge and one sparrow. Although I inoculated these animals repeatedly with very fresh material, I have as yet not been able to infect them with anthrax.

Frogs are also entirely resistant to inoculations with *Bacillus anthracis* or its spores. As I implanted larger pieces of spleen from mice dead from anthrax under the skin of the back in several frogs, and killed and examined the animals after forty-eight hours, the following noteworthy finding was made. The blood of the frogs was entirely free from bacilli. The mouse spleen was slightly adherent to its surroundings and instead of its dark brownish-red color it had assumed a more light grayish-red color. On microscopical examination, unchanged bacilli in large amounts were bound in the centre, but in the outer layers many bacilli were found which had become thicker and more elongated. Between these were found peculiar structures in large number, namely, more or less regular, spirally formed, tortuous bacilli, which were partly free and partly surrounded by a very thin-walled capsule. The explanation for this unusual form of the bacilli is easily to be found when one examines the almost gelatinous outermost surrounding layer of the spleen, apparently excreted by the skin of the frog (Fig. 7). This layer consists of large cells embedded in a structureless viscous ground substance, which almost reach the size of frog's blood corpuscles (Fig. 7a). In spite of their size these are very pale and delicate, have a very distinct nucleus with nucleoli and contain many very small (p. 301) granules engaged in the most lively molecular motion. In most of these cells there were short straight bacilli, in others somewhat curved, cracked bacilli, united in heaps and bundles and, preferably, twisted spirally (Fig. 7b). As soon as the cells harbor several bacilli, the molecular granules in them seem to be enlarged, but if the bacillary proliferation in them predominates, these granules disappear and, finally, also the nucleus which remains recognizable the longest. That the bacilli taken up by the cells as short rods grow in them and after they have filled the interior by the formation of various kinkings and curvatures finally rupture them, is evidenced by the fact, that in addition to the released bacillary spirals (Fig. 7g) and bundles, degenerated and

empty cell membranes are found as the last residua of the destroyed cells (Fig. 7c).*

These bacillus-containing cells are especially beautifully seen if some distilled water is added to the specimen. As a result the cells swell up to some extent, their content becomes more distinct and when they are set in a rolling motion by being torn away by fluid currents, one can easily be convinced that isolated bacilli also actually lie in the interior of the cells and usually close to the nucleus and are not merely compressed into the soft cell surface. The suspicion has been expressed many times, that the amoeboid cells of the animal body may also take up the micrococci that have entered the blood circulation in the same way the white blood cells in an easily demonstrable manner allow pigment granules, artificially introduced into the blood, access into the interior of their protoplasm. As far as I know, up to the present time it has not been possible to differentiate sharply the micrococci from the molecular granules of these cells either by their form or by their reactions. Up to the present time any absolutely certain example of the occurrence of schizophyte-containing living animal cells does not seem to be known. (p. 302) This observation is not an isolated one insofar as I found the same cells in other frogs after putrid dried blood was introduced under the skin of the back; but in this case they contained entirely different shortly geniculated bacilli, which were mostly supplied with a permanent spore (Billroth's heliobacteria). There were also, in addition to numerous free rods, large pale cells in the freshly examined spleen of a horse dead from anthrax (the only one that I had occasion to examine). Most of these cells contained several nuclei and many contained one to ten and more bacilli.

IV. The Etiology of Anthrax. If we review the facts learned up to the present time and if we endeavor to determine the etiology of anthrax with their aid, we must not conceal from our view

* The threads under the frog's skin do not grow longer than medium length and I have never observed the development of spores in them. After several days their number diminishes and they seem to degenerate gradually, but in one frog I have still found long threads and bacilli-containing cells ten days after the transplantation of mouse spleen.

the fact that much is still lacking for an unbroken construction of the etiology. One must not forget, particularly, that all of the animal experiments were conducted on small rodents. It is certainly improbable that the ruminants, the true hosts of the parasite with which we are concerned, should behave very differently from rodents. But there is a difference in the inoculation experiments that small animals die after twenty-four to thirty hours, and large ones only after several days. Could not possibly the bacilli come to spore formation at some site of the animal body during this longer period of time? Or do they never reach spore formation in the living body? Furthermore, the feeding experiments with bacilli and spores in rodents with their negative results are absolutely not decisive for ruminants, the entire digestive process of which is essentially different. Inhalation experiments with spore-bearing masses are still entirely missing. Nor have experiments on the behavior of large anthrax cadavers been made at different temperatures, at different depths of soil and types of soil (argillaceous, chalky, and sandy soil, dry soil, moist soil, and the influence of ground water) in regard to spore formation of the bacilli. It would be of the greatest practical importance to gain definite knowledge in this respect. A number of details regarding the behavior of the bacilli and their spores towards substances that destroy them or hinder their development and regarding the process of their penetration into the blood and lymph vessels would have to be investigated. But even though many a question on the parasites, so puzzling up to the present time has to be answered, (p. 303) its ways of life are open to us to such an extent, that we can definitely determine the etiology of the disease produced by it, at least in the fundamental principles.

Since anthrax substances, regardless of their being relatively fresh, putrescent, or dried or years old, can produce anthrax when these substances contain either bacilli capable of developing or spores of the *Bacillus anthracis*, all doubts as to the *Bacillus anthracis* constituting the actual cause and the contagium of anthrax must be silenced. The transmission of the disease by moist bacilli in very fresh blood rarely occurs in nature, but most

readily in persons, in whom blood or tissue juices gain access to wounds in the act of killing, cutting, and skinning of animals infected with anthrax. Probably the disease is produced more often by dried bacilli which, as has been shown, may retain their effectiveness for a few days, and in favorable cases, for five weeks. When attached to insects, to wool, and the like, together with dust, they may gain access to wounds and then produce the disease. Bacillus-containing masses, which fall into water and are markedly diluted there, very soon lose their effectiveness and probably lead to dissemination of anthrax only exceptionally.

The great mass of the infections, however, which almost always develop under such conditions that the above mentioned methods of transmission must be excluded, can be produced only by the penetration of spores of the *Bacillus anthracis* into the animal body. For the bacilli can maintain themselves viable in a continued dried state only for a short time and can offer resistance neither to moist soil nor to the changing conditions of weather (precipitations and dew). But the spores survive in a hardly believable manner and way. Neither years of dryness, nor existence in a putrescent fluid for months, nor repeated drying and moistening, can destroy their power of germination. When these spores have once formed, there is ample reason for the anthrax not disappearing for a long time in a certain region. It has already been shown that their development is often made possible. A single cadaver, which is handled improperly, can furnish almost innumerable spores and even though millions of these spores degenerate without reaching germination in the blood (p. 304) of an animal, still, because of their great number, the probability is not slight that a few may reach the skin of the animal after a long stay in the soil or in ground water, or on hairs, horns, rags and the like, dried as dust, or may reach the skin of the animal with water and enter the blood circulation directly through a wound. Even later these spores may enter into small abrasions of the skin by rubbing, chafing and scratching of the animal. Possibly they also penetrate into the blood or lymph vessels by way of the air passages or the digestive canal.

If, then, it has been possible to discover the manner of the dis-

semination of anthrax and the conditions under which the contagium constantly renews itself *de novo*, should it not then be possible, in consideration of these conditions, to hinder the contagium, namely, the *Bacillus anthracis*, in its development and so reduce the sickness to the smallest possible incidence and, perhaps, even exterminate it entirely? That this question demands not a little interest, may be seen from the fact that, according to Spinola,* a single Prussian District (Mannsfelder Seekreis) yearly loses 180,000 Marks worth of sheep through anthrax, and that during the years 1867 to 1870 over 56,000 horses, cows and sheep and, besides, 528 persons, lost their lives from anthrax in the Novgorod Government alone.†

The present measures against anthrax are limited to the obligation of notifying the authorities, the burial of the cadavers in moderately deep pits, disinfection, and quarantine of the town affected by the plague. Entirely aside from the fact that we know by experience that only a small number of cases of anthrax is reported because of the extremely annoying rules of quarantine and that in the case of sheep the most widely disseminated anthrax remains almost completely unnoticed and neglected, the burial of the cadaver in the moist soil must, apparently, rather favor the formation of spores and thereby the propagation of the contagium than prevent it. Up to the present time the continued prevention of anthrax in this manner apparently has not been successful anywhere. On the other hand, Oemler‡ reduced his loss of sheep from anthrax from 21 per cent per year to 2 per cent, after he had (p. 305) strictly forbidden the burial of all cadavers, without exception, in fields and pasture grounds.

We must, therefore, seek other measures in order to free the herds from this destroyer and to protect thousands of persons from an agonizing death.

The most certain way would be to destroy all substances that contain the *Bacillus anthracis*. But as it is impossible to carry this out, namely, to make innocuous this amount of cadavers, such

* Pappenheim, Sanitätspolizei, 2: 276.

† Grimm (Virchow's Archiv., 54: 262) cited from Bollinger, Ibid., page 469.

‡ Bollinger, Ibid., page 453.

as anthrax provides, by chemicals or boiling heat, or even to do away with them by burning, we must abandon this radical measure. If it would only be possible to hinder the bacilli from developing spores or, at least, reduce this to a minimum, the infections with anthrax would constantly diminish in number and finally disappear.

Because the bacilli, as we have seen, require the access of air, moisture and a higher temperature of about 15 degrees C. for the formation of spores, it must suffice to deprive them of one of these conditions in order to prevent them from further development. The rapid drying of large cadavers would require special apparatus and itself would cause difficulties greater than burning. Instead of this, one could, without much trouble and cost, cool the anthrax cadaver for a considerable time, even in the summer time, below 15 degrees, at the same time limit the access of oxygen and in this way cause the bacilli to die. Particularly, if one considers that in Middle Europe, namely in Germany, an almost constant temperature prevails at an 8 to 10 meter depth of the soil, which very closely approaches the year's average and hence in every case remains below 15 degrees C., it would be necessary only to dig spacious wells or pits of this depth and to sink the anthrax cadavers in them to destroy the bacilli and thereby make the cadaver innocuous. Such pits would have to be dug in certain districts in smaller or greater number according to the average number of cases of anthrax. These pits would be located at a moderate distance from the farm buildings and, naturally, supplied with a secure enclosure. In this way one would at the same time have an advantage which is not to be undervalued that the cadaver would not be recovered during the night, cut up, and disseminated all around. As usually happens at present and as I know from my own experience, the anthrax cadavers buried according to regulations or even against them are regularly stolen by thieves (often enough by the same people (p. 306) as had buried them during the day).

It is also possible that the influence of certain types of soil or a certain lack of moisture and of a deep ground water prevents the development of spores. This points to the occurrence of anthrax

in certain districts and its subsidence after extensive improvements and drainages.

The case reported by Buhl,* in which the anthrax among horses disappeared completely in the stud NeuhoF at Donauwörth when, at the advice of Counsellor von Pettenkofer the depth of the ground water was lowered by drainage, would likewise fall in this category.

At any rate, there is the possibility of preventing the development of anthrax spores. The great interest that this matter demands should urgently lead to further attempts in the direction mentioned at suitable experimental stations.

I also add an observation, which I have made in this region on the occurrence of anthrax, because it is well worthy of consideration in the prophylaxis of anthrax. It is indeed striking that anthrax prevails through the whole year among sheep almost without interruption. In the larger herds many sheep are almost never affected at one time, but usually isolated ones, and often at great intervals of time, so that several months, half a year or a longer time, intervene between the individual cases. In this region anthrax occurs exceptionally among horses. It appears, therefore, that the sheep is the true host of the *Bacillus anthracis* and that only under exceptional circumstances does it occasionally affect other species of animals. This view is supported by the observation of Leonhardt,† that in Bönstadt, which suffered much from anthrax, the latter almost completely disappeared among the cattle, after the sheep that were infected by anthrax in greater numbers during the summer had been removed. This leads to the conclusion, that in all measures against this pestilence, anthrax deserves the greatest consideration among the herds of sheep.

V. The Comparison of Anthrax with Other Diseases. Owing to the fact that anthrax has been traced to its true causes, it has been possible for the first time to (p. 307) shed light on the etiology of those remarkable diseases, which depend on conditions of the soil. Up to the present time it has not been possible to explain

* Bollinger, *Ibid.*, page 455.

† Bollinger, *Ibid.*, p. 453.

these sufficiently either by the application of investigation or the boldest complicated hypotheses. Therefore it is very important to make a comparison between anthrax and the diseases closely allied to it by its method of dissemination, particularly with typhoid fever and cholera.

Anthrax resembles typhoid fever in its dependence upon ground water, its preference for lowlands, its sporadic appearance throughout the entire year, and the associated increase in the number of cases to an epidemic in the late summer. The first of the above mentioned points applies also to cholera; but in one respect the contagium of cholera in such a peculiar manner corresponds with that of anthrax that the assumption of a pure accident must be excluded. Von Pettenkofer has called attention to the fact, that on ships the contagium of cholera, when these do not touch land, usually dies out in three to four weeks, and only when it reaches suitable soil before this time, can the disease spread any further. Let us assume, for example, that anthrax is a disease that is indigenous in India, and that animals infected with this disease could reach us only after a four to five weeks' sea trip. Then, just as in the case of cholera, a dissemination on the sea voyage could not be possible, as no spores could develop because of the lack of moist soil. The bacilli possibly dried on objects would have died off before the end of the trip. If we further assume that anthrax is a disease which is not produced by large bacilli, but by other extraordinarily small schizophytes at the limit of visibility, which would exert their deleterious effect not freely in the blood, but (like the bacilli in the horse spleen) secretly in the white blood cells, in the cells of the lymph nodes, and in the spleen, then we would have to admit a still much closer relationship with the contagium of cholera and typhoid fever. As a matter of fact, no substance would have a greater similarity to the contagium of this disease than such a contagium of anthrax.

With such observations there arises the hope that the typhoid and the cholera contagium will also be found in the form of spherical bacteria or similar schizophytes. (p. 308) But the most serious doubts oppose this hope. Provided that these diseases depend upon a visible contagium, it must be assumed that it is not

visible, or only so with difficulty, with our optical aids, as many of the experienced microscopists have until now looked for it in vain. Should such a contagium be found we would then still lack the one means, as typhoid fever and cholera cannot be transmitted to animals, of convincing ourselves of the identity of the schizophytes. Their outer forms have so little that is characteristic, that which makes the investigations on the contagium of anthrax so simple and so certain, namely, the unmistakable form of the bacilli and the control carried on by inoculation, would be lacking for typhoid fever and cholera. Nevertheless, we must not be deterred by the obstacles which at present seem indomitable from striving for the goal, so far as our present aids allow. But one must not begin, as heretofore, with the most difficult. At first, only the obvious, which can be reached with our aids, should be investigated.

We must allow the way to the more remote and inaccessible findings to be shown to us by the results and methods of investigation gained in this way. The provisional attainment in this field is the etiology of the infectious diseases of animals and of human diseases which, like diphtheria, can be transmitted to animals. These diseases give us the opportunity of supplementing the microscope with the animal experiment since that instrument no longer has sufficient power for these investigations.

Only with the aid of such an acquired comparative etiology of the infectious diseases will it be possible to fathom the nature of the epidemic diseases which affect the human race frequently and severely, and to find sure remedies to control them.

Wollstein, Grand Ducy of Posen, May 27, 1876.

EXPLANATION OF ILLUSTRATIONS

PLATE XI

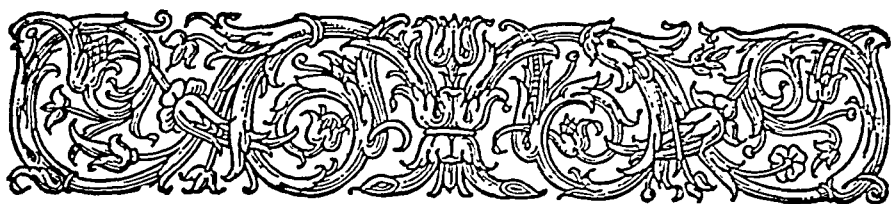
ONTOGENESIS OF THE BACILLUS

Figs. 1-7 Anthrax Bacilli (*Bacillus Anthracis*)

Fig. 1. Anthrax bacilli from the blood of a guinea-pig; the bacilli as transparent rods, some with beginning transverse division or kinked, (a) white, (b) red blood cells.

- Fig. 2. Anthrax bacilli from the spleen of a mouse, after 3 hours' culture in a drop of aqueous humor; growing from threads, elongated 3 to 8 times, some kinked and curved.
- Fig. 3. Microscopical field from the same specimen after 10 hours' culture; the bacilli grown into long threads, which are often wound around one another in bundles; (a) more markedly transparent granules appear in some threads at regular distances.
- Fig. 4. Microscopical field from the same specimen after 24 hours' culture; (a) longitudinally round spores have developed in the threads like a string of pearls at regular distances; (b) some threads are in the act of dissolving, the spores free, isolated, or conglomerated in heaps.
- Fig. 5. Germination of the spores; (a) with Hartnack Immersion 9 drawn by Koch, (b) with Seibert Immersion VIII drawn by Cohn. The spore elongates into a cylindric body, the markedly refractive mass remains at one pole, becomes smaller, breaks up into 2 or more parts, and finally disappears entirely.
- Fig. 6. Representation of the culture of anthrax bacilli in a hollow ground glass slide, covered with a cover glass, closed air tight by means of olive oil painted all around and warmed by means of an M. Schulze stage to blood heat; natural size. The bacilli are located in a drop of fresh aqueous humor; even with the naked eye one recognizes the lightly floating extremely delicate masses of threads, proliferated into the drop from the site of the dissemination.
- Fig. 7. Microscopical field from the surrounding layer of a small piece from the spleen of a mouse dead from anthrax introduced under the skin of the back of a frog; this layer consists of large, nucleated cells (a); isolated cells have taken up numerous small, somewhat kinked or curved bacilli grouped into heaps or twisted spirally (b); which continue to grow in the cells and, finally, rupture them; (c) degenerated cell membranes, (g) liberated spirals of bacilli; (e) blood corpuscles of the frog; unchanged bacilli are also visible.

Figures 1 to 7 are drawn from anthrax bacilli (*Bacillus anthracis*) by Dr. Koch. Magnification of Figs. 1 to 7 is 650 (drawn with Hartnack immersion IX, of Fig. 5b 1650 (drawn with Seibert immersion VIII).



I. Die Aetiologie der Tuberculose

VON

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(Nach einem in der physiologischen Gesellschaft zu Berlin am 24. März cr. gehaltenen Vortrage) *Berliner Klinische Wochenschrift*, 19: 221–230, 1882

DIE von Villemain gemachte Entdeckung, dass die Tuberculose auf Thiere übertragbar ist, hat bekanntlich vielfache Bestätigung, aber noch anscheinend wohlbegründeten Widerspruch gefunden, so dass es bis vor wenigen Jahren unentschieden bleiben musste, ob die Tuberculose eine Infectiouskrankheit sei oder nicht. Seitdem haben aber die zuerst von Cohnheim und Salomonsen, später von Baumgarten ausgeführten Impfungen in die vordere Augenkammer, ferner die Inhalationsversuche von Tappeiner und Anderen die Uebertragbarkeit der Tuberculose gegen jeden Zweifel sicher gestellt und es muss ihr in Zukunft ein Platz unter den Infectiouskrankheiten angewiesen werden.

Wenn die Zahl der Opfer, welche eine Krankheit fordert, als Massstab für ihre Bedeutung zu gelten hat, dann müssen alle Krankheiten, namentlich aber die gefürchtetsten Infectiouskrankheiten, Pest, Cholera u. s. w. weit hinter der Tuberculose zurückstehen. Die Statistik lehrt, dass $\frac{1}{4}$ aller Menschen an Tuberculose stirbt und dass, wenn nur die mittleren productiven Altersklassen in Betracht kommen, die Tuberculose ein Drittel derselben und oft mehr dahinrafft. Die öffentliche Gesundheitspflege hat also Grund genug, ihre Aufmerksamkeit einer so

mörderischen Krankheit zu widmen, ganz abgesehen davon, dass noch andere Verhältnisse, von denen nur die Beziehungen der Tuberculose zur Perlsucht erwähnt werden sollen, das Interesse der Gesundheitspflege in Anspruch nehmen.

Da es nun zu den Aufgaben des Gesundheitsamtes gehört, die Infectionskrankheiten vom Standpunkte der Gesundheitspflege aus, also in erster Linie in Bezug auf ihre Aetiologie, zum Gegenstand von Ermittlungsarbeiten zu machen, so erschien es als eine dringende Pflicht, von Allem über die Tuberculose eingehende Untersuchungen anzustellen.

Das Wesen der Tuberculose zu ergründen, ist schon wiederholt versucht, aber bis jetzt ohne Erfolg. Die zum Nachweis der pathogenen Microorganismen so vielfach bewährten Färbungsmethoden haben dieser Krankheit gegenüber im Stich gelassen und die zum Zwecke der Isolirung und Züchtung des Tuberkel-Virus angestellten Versuche konnten bis jetzt nicht als gelungen angesehen werden, so dass Cohnheim in der soeben erschienenen neuesten Auflage seiner Vorlesungen über allgemeine Pathologie „den directen Nachweis des tuberculösen Virus als ein bis heute noch ungelöstes Problem“ bezeichnen musste.

Bei meinen Untersuchungen über die Tuberculose habe ich mich anfangs auch der bekannten Methoden bedient, ohne damit eine Aufklärung über das Wesen der Krankheit zu erlangen. Aber durch einige gelegentliche Beobachtungen wurde ich dann veranlasst, diese Methoden zu verlassen und andere Wege einzuschlagen, die schliesslich auch zu positiven Resultaten führten.

Das Ziel der Untersuchung musste zunächst auf den Nachweis von irgend welchen, dem Körper fremdartigen, parasitischen Gebilden gerichtet sein, die möglicherweise als Krankheitsursache gedeutet werden konnten. Dieser Nachweis gelang auch in der That durch ein bestimmtes Färbungsverfahren, mit Hülfe dessen in allen tuberculös veränderten Organen charakteristische, bis dahin nicht bekannte Bakterien zu finden waren. Es würde zu weit führen, den Weg, auf welchem ich zu diesem neuen Verfahren gelangte, zu schildern und ich will deswegen sofort zur Beschreibung desselben übergehen.

Die Untersuchungsobjecte werden in der bekannten, für

Untersuchungen auf pathogene Bacterien üblichen Weise, vorbereitet und entweder auf dem Deckglas ausgebreitet, getrocknet und erhitzt, oder nach Erhärtung in Alkohol in Schnitte zerlegt. Die Deckgläschen oder Schnitte gelangen in eine Farblösung von folgender Zusammensetzung. 200 Ccm. destillirten Wassers werden mit 1 Ccm. einer concentrirten alcoholischen Methylenblau-Lösung vermischt, umgeschüttelt und erhalten dann unter wiederholtem Schütteln noch einen Zusatz von 0,2 Ccm. einer 10% Kalilauge. Diese Mischung darf selbst nach tagelangem Stehen keinen Niederschlag geben. Die zu färbenden Objecte bleiben in derselben 20 bis 24 Stunden. Durch Erwärmen der Farblösung auf 40°C. im Wasserbade kann diese Zeit auf $\frac{1}{2}$ bis 1 Stunde abgekürzt werden. Die Deckgläschen werden hierauf mit einer concentrirten wässrigen Lösung von Vesuvin, welche vor jedesmaligem Gebrauche zu filtriren ist, übergossen und nach ein bis zwei Minuten mit destillirtem Wasser abgespült. Wenn die Deckgläschen aus dem Methylenblau kommen, sieht die ihnen anhaftende Schicht dunkelblau aus und ist stark (p. 222) überfärbt, durch die Behandlung mit dem Vesuvin geht die blaue Farbe derselben verloren und sie erscheint schwach braun gefärbt. Unter dem Microscop zeigen sich nun alle Bestandtheile thierischer Gewebe, namentlich die Zellkerne und deren Zerfallsproducte braun, die Tuberkelbakterien dagegen schön blau gefärbt. Auch alle anderen bis jetzt von mir darauf hin untersuchten Bacterien, mit Ausnahme der Leprabacillen, nehmen bei diesem Färbungsverfahren eine braune Farbe an. Der Farbencontrast zwischen dem braun gefärbten Gewebe und den blauen Tuberkelbakterien ist so auffallend, dass letztere, welche oft nur in sehr geringer Zahl vorhanden sind, trotzdem mit der grössten Sicherheit aufzufinden und als solche zu erkennen sind.

Ganz ähnlich sind die Schnitte zu behandeln. Sie werden aus der Methylenblau-Lösung in die filtrirte Vesuvinlösung gebracht, bleiben darin 15 bis 20 Minuten und werden dann in destillirtem Wasser so lange gespült, bis die blaue Farbe geschwunden und eine mehr oder weniger stark braune Tinction zurückgeblieben ist. Hiernach entwässert man sie mit Alkohol, hellt sie in Nelkenöl auf und kann sie sofort in dieser Flüssigkeit micro-

scopisch untersuchen oder auch schliesslich in Canada-balsam einlegen. In diesen Präparaten erscheinen ebenfalls die Gewebsbestandtheile braun und die Tuberkelbakterien lebhaft blau gefärbt.

Uebrigens sind die Bakterien nicht etwa ausschliesslich mit Methylenblau zu färben, sondern sie nehmen mit Ausnahme von braunen Farbstoffen auch andere Ainfarben unter der gleichzeitigen Einwirkung von Alkalien auf, doch fällt die Färbung bei Weitem nicht so schön aus wie mit Methylenblau. Ferner kann bei dem angegebenen Färbungsverfahren die Kalilösung durch Natron oder Ammoniak ersetzt werden, woraus zu schliessen ist, dass nicht etwa dem Kali an sich dabei eine wesentliche Rolle zufällt, sondern dass es nur auf die stark alkalische Beschaffenheit der Lösung ankommt. Dafür spricht auch, dass durch einen noch stärkeren Kalizusatz die Bakterien noch an Stellen gefärbt werden können, wo sie mit einer weniger kalihaltigen Lösung nicht mehr zum Vorschein kommen. Doch schrumpfen die Gewebstheile des Schnittpräparates und verändern sich unter dem Einfluss stärkerer Kalilösungen so sehr, dass letztere nur ausnahmsweise von Vortheil sein werden.

Die durch dieses Verfahren sichtbar gemachten Bakterien zeigen ein in mancher Beziehung eigenthümliches Verhalten. Sie haben eine stäbchenförmige Gestalt und gehören also zur Gruppe der Bacillen. Sie sind sehr dünn und ein viertel bis halb so lang als der Durchmesser eines rothen Blutkörperchens beträgt, mitunter können sie auch eine grössere Länge, bis zum vollen Durchmesser eines Blutkörperchens, erreichen. Sie besitzen in Bezug auf Gestalt und Grösse eine auffallende Aehnlichkeit mit den Leprabacillen. Doch unterscheiden sich letztere von ihnen dadurch, dass sie ein wenig schlanker und an den Enden zugespitzt erscheinen. Auch nehmen die Leprabacillen bei dem Weigert'schen Kernfärbungsverfahren den Farbstoff an, was die Tuberkelbacillen nicht thun. An allen den Punkten, wo der tuberculöse Process in frischem Entstehen und in schnellem Fortschreiten begriffen ist, sind die Bacillen in grosser Menge vorhanden; sie bilden dann gewöhnlich dicht zusammengedrängte und oft bündelartig angeordnete kleine Gruppen,

welche vielfach im Innern von Zellen liegen und stellenweise eben solche Bilder geben, wie die in Zellen angehäuften Lepra-bacillen. Daneben finden sich aber auch zahlreiche freie Bacillen. Namentlich am Rande von grösseren käsigen Herden kommen fast nur Schaaren von Bacillen vor, die nicht in Zellen eingeschlossen sind.

Sobald der Höhepunkt der Tuberkeleruption überschritten ist, werden die Bacillen seltener, finden sich nur noch in kleinen Gruppen oder ganz vereinzelt am Rande des Tuberkelherdes neben schwach gefärbten und mit unter kaum noch erkennbaren Bacillen, welche vermuthlich im Absterben begriffen oder schon abgestorben sind. Schliesslich können sie ganz verschwinden, doch fehlen sie vollständig nur selten und dann auch nur an solchen Stellen, an denen der tuberculöse Process zum Stillstand gekommen ist.

Wenn in dem tuberculösen Gewebe Riesenzellen vorkommen, dann liegen die Bacillen vorzugsweise im Innern dieser Gebilde. Bei sehr langsam fortschreitenden tuberculösen Processen ist das Innere der Riesenzellen gewöhnlich die einzige Stätte, wo die Bacillen zu finden sind. In diesem Falle umschliesst die Mehrzahl der Riesenzellen einen oder wenige Bacillen und es macht einen überraschenden Eindruck, in weiten Strecken des Schnittpräparates immer neuen Gruppen von Riesenzellen zu begegnen, von denen fast jede einzelne in dem weiten, von braungefärbten Kernen umschlossenen Raum ein oder zwei winzige, fast im Centrum der Riesenzelle schwebende, blau-gefärbte Stäbchen enthält. Oft sind die Bacillen nur in kleinen Gruppen von Riesenzellen, selbst nur in einzelnen Exemplaren anzutreffen, während gleichzeitig viele andere Riesenzellen frei davon sind. Dann sind die bacillenhaltigen, wie aus ihrer Grösse und Lage zu schliessen ist, die jüngeren Riesenzellen, die bacillenfreien dagegen die älteren und es lässt sich annehmen, dass auch die letzteren ursprünglich Bacillen umschlossen, dass diese aber abgestorben oder in den bald zu erwähnenden Dauerzustand übergegangen sind. Nach Analogie der von Weiss, Friedlaender und Laulamié beobachteten Bildung von Riesenzellen um Fremdkörper, wie Pflanzenfasern und Strongyluseier,

wird man sich das Verhältniss der Riesenzellen zu den Bacillen so vorstellen können, dass auch hier die Bacillen als Fremdkörper von den Riesenzellen eingeschlossen werden und deswegen ist selbst dann, wenn die Riesenzelle leer gefunden wird, alle übrigen Verhältnisse aber auf tuberculöse Processe deuten, die Vermuthung gerechtfertigt, dass sie früher einen oder mehrere Bacillen beherbergt hat und diese zu ihrer Eutstehung Veranlassung gegeben haben.

Auch ungefärbt in unpräparirtem Zustande sind die Bacillen der Beobachtung zugänglich. Es ist dazu erforderlich, von solchen Stellen, welche bedeutende Mengen von Bacillen enthalten, z. B. von einem grauen Tuberkelknötchen aus der Lunge eines an Impftuberculose gestorbenen Meerschweinchens ein wenig Substanz unter Zusatz von destillirtem Wasser oder besser Blutserum zu untersuchen, was, um Strömungen in der Flüssigkeit zu vermeiden, am zweckmässigsten im hohlen Objectträger geschieht. Die Bacillen erscheinen dann als sehr feine Stäbchen, welche nur Molecularbewegung zeigen, aber nicht die geringste Eigenbewegung besitzen.

Unter gewissen später zu erwähnenden Verhältnissen bilden die Bacillen schon im thierischen Körper Sporen und zwar enthalten die einzelnen Bacillen mehrere, meistens 2 bis 6 Sporen, von ovaler Gestalt, welche in gleichmässigen Abständen auf die Länge des Bacillus vertheilt sind.

In Bezug auf das Vorkommen der Bacillen bei den verschiedenen tuberculösen Erkrankungen des Menschen und der Thiere konnte bis jetzt folgendes Material untersucht werden:

I) Vom Menschen: 11 Fälle von Miliartuberculose. Die Bacillen wurden in den Miliartuberkeln der Lungen niemals vermisst; oft waren allerdings in solchen Knötchen, deren Centrum keine Kernfärbung mehr annimmt, auch keine Bacillen mehr zu finden, dann waren sie aber am Rande des Tuberkels noch in kleinen Gruppen Vorhanden und in jüngeren, noch nicht im Centrum verkästen Knötchen in um so grösserer Menge zu (p. 223) finden. Sie konnten ausser in den Lungen auch in den Miliar-tuberkeln der Milz, Leber und Niere nachgewiesen werden. Sehr reichlich fanden sie sich in den grauen Knötchen der Pia

mater bei Meningitis basilaris. Auch die bei mehreren Fällen untersuchten verkästen Bronchialdrüsen enthielten zum Theil dichte Schwärme von Bacillen und darunter viele sporenhaltige, zum Theil in das Drüsengewebe eingebettete Tuberkel mit einer von epitheloiden Zellen umgebenen Riesenzelle im Centrum und im Innern der Riesenzelle einige Bacillen.

12 Fälle von käsiger Bronchitis und Pneumonie (in 6 Fällen Cavernenbildung). Das Vorkommen der Bacillen beschränkte sich meistens auf den Rand des Käsig infiltrirten Gewebes, war daselbst aber mehrfach ein sehr reichliches. Auch im Innern der infiltrirten Lungenpartien trifft man bisweilen auf Bacillennester. Ungemein zahlreich finden sich die Bacillen in den meisten Cavernen. Die bekannten kleinen käsigen Bröckchen im Caverneninhalt bestehen fast ganz aus Bacillenmassen. Unter den Bacillen, welche in den käsig erweichten Herden und in den Cavernen sich befinden, wurden einige Male zahlreiche mit Sporen versehene angetroffen. In grösseren Cavernen kommen sie mit anderen Bakterien vermischt vor, waren aber leicht von diesen zu unterscheiden, weil bei der angegebenen Färbungsmethode nur die Tuberkelbacillen die blaue Tinction behalten, die anderen Bakterien, wie schon erwähnt wurde, eine braune Farbe annehmen.

1 Fall von solitärem, mehr als haselnussgrossen Tuberkel des Gehirns. Die käsige Masse des Tuberkels war von einem zellenreichen Gewebe eingeschlossen, in welches viele Riesenzellen sich eingebettet fanden. Die meisten Riesenzellen enthielten keine Parasiten, aber stellenweise traf man Gruppen von Riesenzellen, von denen jede einen oder auch zwei Bacillen enthielt.

2 Fälle von Darmtuberculose. In den Tuberkelknötchen, welche sich um die Darmgeschwüre gruppirten, konnten die Bacillen besonders gut nachgewiesen werden und zwar fanden sie sich auch hier wieder vorzugsweise zahlreich in den jüngsten und kleinsten Knötchen. In den zu diesen beiden Fällen gehörigen Mesenterialdrüsen waren die Bacillen ebenfalls in grosser Menge vorhanden.

3 Fälle von frisch exstirpirten scrophulösen Drüsen. Nur in zweien derselben konnten in Riesenzellen eingeschlossene Bacillen nachgewiesen werden.

4 Fälle von fungöser Gelenksentzündung. In zwei Fällen wurden ebenfalls nur in vereinzelt kleinen Gruppen von Riesenzellen Bacillen gefunden.

II) Von Thieren: 10 Fälle von Perlsucht mit verkalkten Knoten in den Lungen, mehrfach auch im Peritoneum und einmal am Pericardium. In sämtlichen Fällen fanden sich die Bacillen und zwar vorwiegend im Innern von Riesenzellen, welche in dem die kalkigen Massen umschliessenden Gewebe sich befinden. Die Vertheilung der Bacillen ist meistens eine so gleichmässige, dass unter zahlreichen Riesenzellen kaum eine zu finden ist, welche nicht einen oder mehrere, mitunter bis zu 20 Bacillen umschliesst. In einem dieser Fälle konnten die Bacillen zugleich in den Bronchialdrüsen und in einem zweiten in den Mesenterialdrüsen nachgewiesen werden.

3 Fälle, in denen die Lungen von Rindern nicht die bekannten verkalkten, mit höckriger Oberfläche versehenen Knoten der gewöhnlichen Perlsucht, sondern glattwandige, mit dickbreiiger, käseartiger Masse gefüllte, kuglige Knoten enthielten. Gewöhnlich wird diese Form nicht zur Tuberculose gerechnet, sondern als eine Bronchiectasis aufgefasst. Auch in der Umgebung dieser Knoten fanden sich Riesenzellen und in diesen die Tuberkelbacillen.

Eine verkäste Hals-Lymphdrüse vom Schwein enthielt ebenfalls die Bacillen.

In den Organen eines an Tuberculose gestorbenen Huhnes und zwar sowohl in den Tuberkelknoten des Knochenmarks, als in den eigenthümlichen grossen Knoten des Darms, der Leber und Lunge befanden sich grosse Mengen von Tuberkelbacillen.

Von 3 spontan an Tuberculose gestorbenen Affen wurden die mit unzähligen Knötchen durchsetzten Lungen, Milz, Leber Netz und die verkästen Lymphdrüsen untersucht und überall in den Knötchen oder deren nächsten Umgebung die Bacillen gefunden.

Von spontan erkrankten Thieren kamen noch 9 Meerschweinchen und 7 Kaninchen zur Untersuchung, welche ebenfalls sämtlich in den Tuberkelknötchen die Bacillen aufwiesen.

Ausser diesen Fällen von spontaner Tuberculose stand mir

noch eine nicht unbedeutende Zahl von Thieren zur Verfügung, welche durch Impfung mit den verschiedensten tuberculösen Substanzen inficirt waren, nämlich mit grauen und verkästen Tuberkeln menschlicher Lungen, mit Sputum von Phthisikern, mit Tuberkelmassen von spontan erkrankten Affen, Kaninchen und Meerschweinchen, mit Massen aus verschiedenen sowohl verkalkten, als auch käsigen perlsüchtigen Rinderlungen und schliesslich auch durch Weiterimpfung der in dieser Weise erhaltenen tuberculösen Affectionen. Die Zahl der so inficirten Thiere belief sich auf 172 Meerschweinchen, 32 Kaninchen und 5 Katzen. Der Nachweis der Bacillen musste sich in der Mehrzahl dieser Fälle auf die Untersuchung der immer in grosser Menge vorhandenen Tuberkelknötchen der Lungen beschränken. In diesen wurden die Bacillen nicht ein einziges Mal vermisst; oft waren sie ausserordentlich zahlreich, mitunter auch sporenhaltig, aber nicht selten waren sie in den angefertigten Präparaten auch nur in wenigen, jedoch unzweifelhaften Exemplaren zuzufinden.

Bei der Regelmässigkeit des Vorkommens der Tuberkelbacillen muss es auffallend erscheinen, dass sie bisher von Niemandem gesehen sind. Doch erklärt sich dies daraus, dass die Bacillen ausserordentlich kleine Gebilde und meistens so spärlich an Zahl sind, namentlich wenn sich ihr Vorkommen auf das Innere der Riesenzellen beschränkt, dass sie schon aus diesem Grunde ohne ganz besondere Farbenreactionen dem aufmerksamsten Beobachter entgehen müssen. Wenn sie sich aber auch in grösseren Mengen beisammen finden, sind sie mit feinkörnigem Detritus in einer Weise untermengt und dadurch verdeckt, dass auch dann ihr Erkennen im höchsten Grade erschwert ist.

Uebrigens existiren einige Angaben über Befunde von Microorganismen in tuberculös veränderten Geweben. So erwähnt Schüller in seiner Schrift über scrophulöse und tuberculöse Gelenkleiden, dass er constant Micrococcen gefunden habe. Zweifellos muss es sich dabei, ebenso wie bei den von Klebs in Tuberkeln gefundenen kleinsten beweglichen Körnchen um etwas anderes, als die von mir gesehenen Tuberkelbacillen, welche unbeweglich und stäbchenförmig sind, gehandelt haben. Ferner

hat Aufrecht, wie er in dem ersten Heft seiner pathologischen Mittheilungen berichtet, unter einer Anzahl von Kaninchen, welche er mit perlsüchtigen oder tuberculösen Substanzen infectirt hatte, bei drei von diesen Thieren im Centrum der Tuberkelknötchen neben zwei verschiedenen Micrococcusarten auch kurze stäbchenförmige Gebilde gefunden, deren Längsdurchmesser den Querdurchmesser nur um die Hälfte übertraf. Die Tuberkelbacillen sind aber mindestens 5 Mal so lang als dick, oft noch viel länger im Verhältniss zur Dicke, ausserdem kommen sie bei reiner Tuberculose niemals mit Micrococcen oder anderen Bakterien vermengt im Tuberkel vor. Es ist deswegen ausserordentlich unwahrscheinlich, dass Aufrecht die wirklichen (p. 224) Tuberkelbacillen gesehen hat; wäre es der Fall, dann hätte er auch in menschlichen Tuberkeln und in der Perlsucht-lunge die Bacillen nachweisen müssen und es hätte ihm das auffallende Verhältniss zwischen Bacillen und Riesenzellen nicht entgehen können.

Auf Grund meiner zahlreichen Beobachtungen halte ich es für erwiesen, dass bei allen tuberculösen Affectionen des Menschen und der Thiere constant die von mir als Tuberkelbacillen bezeichneten und durch charakteristische Eigenschaften von allen anderen Microorganismen sich unterscheidenden Bakterien vorkommen. Aus diesem Zusammentreffen von tuberculöser Affection und Bacillen folgt indessen noch nicht, dass diese beiden Erscheinungen in einem ursächlichen Zusammenhange stehen, obwohl ein nicht geringer Grad von Wahrscheinlichkeit für diese Annahme sich aus dem Umstande ergibt, dass die Bacillen sich vorzugsweise da finden, wo der tuberculöse Process im Entstehen oder Fortschreiten begriffen ist, und dort verschwinden, wo die Krankheit zum Stillstand kommt.

Um zu beweisen, dass die Tuberculose eine durch die Einwanderung der Bacillen veranlasste und in erster Linie durch das Wachsthum und die Vermehrung derselben bedingte parasitische Krankheit sei, mussten die Bacillen vom Körper isolirt, in Reinculturen so lange fortgezüchtet werden, bis sie von jedem etwa noch anhängenden, dem thierischen Organismus

entstammenden Krankheitsprodukt befreit sind, und schliesslich durch die Uebertragung der isolirten Bacillen auf Thiere dasselbe Krankheitsbild der Tuberculose erzeugt werden, welches erfahrungsgemäss durch Impfung mit natürlich entstandenen Tuberkelstoffen erhalten wird.

Mit Uebergehung der vielen Vorversuche, welche zur Lösung dieser Aufgabe dienten, soll auch hier wieder die fertige Methode geschildert werden. Das Princip derselben beruht auf der Verwerthung eines festen durchsichtigen Nährbodens, welcher auch bei Bruttemperatur seine feste Consistenz behält. Die Vortheile dieser von mir in die Bakterienforschung eingeführten Methode der Reincultur habe ich in einer früheren Publication ausführlich auseinandergesetzt. Dass durch dieselbe die Lösung der gewiss nicht einfachen Aufgabe, die Tuberkelbacillen rein zu cultiviren, erreicht wurde, ist mir ein neuer Beweis für die Leistungsfähigkeit dieser Methode.

Serum von Rinder- oder Schafblut, welches möglichst rein gewonnen ist, wird in durch Wattepfropf verschlossene Reagensgläschen gefüllt und sechs Tage hindurch täglich eine Stunde lang auf 58° C. erwärmt. Durch dieses Verfahren gelingt es, wenn auch nicht immer, so doch in den meisten Fällen, das Serum vollkommen zu sterilisiren. Dann wird es auf 65° C. mehrere Stunden hindurch und zwar so lange erwärmt, bis es eben erstarrt und fest geworden ist. Das Serum erscheint nach dieser Behandlung als eine bernsteingelbe, vollkommen durchscheinende oder nur schwach opalescirende, fest gallertartige Masse und darf, wenn es sich mehrere Tage lang in Bruttemperatur befindet, nicht die geringste Entwicklung von Bakteriencolonien zeigen. Geht die Erhitzung über 75° hinaus, oder dauert sie zu lange, dann wird das Serum undurchsichtig. Um eine grosse Fläche zur Anlage der Culturen zu erhalten, lässt man das Serum bei einer möglichst geneigten Lage der Reagensgläser erstarren. Für solche Culturen, welche der unmittelbaren microscopischen Untersuchung zugänglich gemacht werden sollen, wird das Serum in flachen Uhrgläschen oder in hohlen Glasklätzchen zum Erstarren gebracht.

Auf dieses erstarrte Blutserum, welches einen durchsichtigen, bei Bruttemperatur fest bleibenden Nährboden bildet, werden die tuberculösen Substanzen und zwar in folgender Weise gebracht.

Der einfachste Fall, in welchem das Experiment fast ohne Ausnahme gelingt, ist gegeben, wenn ein soeben an Tuberculose gestorbenes, oder ein zu diesem Zwecke getödtetes tuberculöses Thier zur Verfügung steht. Zuerst wird die Haut mit kurz vorher ausgeglühten Instrumenten über Brust und Bauch zur Seite gelegt. Mit einer ebenfalls geglühten Scheere und Pincette werden alsdann die Rippen in der Mitte durchschnitten, die Vorderwand des Brustkorbes, ohne dass die Bauchhöhle dabei eröffnet wird, entfernt, so dass die Lungen zu einem grossen Theil freigelegt sind. Die Instrumente sind nun nochmals mit anderen eben desinficirten zu vertauschen, einzelne Tuberkelknötchen oder Partikelchen derselben von der Grösse eines Hirsekornes mit der Scheere schnell aus dem Lungengewebe herauszupräpariren und sofort mit einem kurz vorher ausgeglühten, in einen Glasstab eingeschmolzenen Platindraht in das Reagensglas auf die Fläche des erstarrten Blutserum zu übertragen. Selbstverständlich darf der Wattepfropf nur möglichst kurze Zeit gelüftet werden. In dieser Weise werden eine Anzahl Reagensgläser, etwa sechs bis zehn an der Zahl mit Tuberkelsubstanz versehen, weil selbst bei der vorsichtigsten Manipulation nicht alle Gläser frei von zufälligen Verunreinigungen bleiben.

Lymphdrüsen, die in beginnender Verkäsung sich befinden, eignen sich ebenso gut zu diesem Experiment, wie Lungentuberkel; weniger gut dagegen der Eiter aus geschmolzenen Lymphdrüsen, welcher meistens nur sehr wenige oder gar keine Bacillen enthält.

Schwieriger ist die Cultur der Bacillen unmittelbar aus menschlichen tuberculösen Organen, oder aus perlsüchtiger Lunge. Ich habe Objecte dieser Art, deren Entnahme aus dem Körper ich nicht selbst mit den vorher erwähnten Vorsichtsmassregeln besorgen konnte, sorgfältig und wiederholt mit Sublimatlösung abgewaschen, dann die oberflächlichen Schichten mit geglühten Instrumenten abgetragen und die Impfsubstanz aus einer Tiefe

genommen, von der sich erwarten liess, dass Fäulnisbakterien bis dahin noch nicht gedrungen sein konnten.

Die in der geschilderten Weise mit Tuberkelsubstanz versehenen Reagensgläschen kommen in den Brutapparat und müssen dauernd bei einer Temperatur von 37 bis 38° C. gehalten werden. In der ersten Woche ist keine merkliche Veränderung zu bemerken. Tritt eine solche ein und bilden sich schon in den ersten Tagen etwa von der Impfsubstanz ausgehend oder gar entfernt von derselben schnell um sich greifende Bacterienwucherungen, die sich gewöhnlich als weisse, graue oder gelbliche Tropfen, oft auch unter Verflüssigung des festen Blutserum, zu erkennen geben, so handelt es sich um Verunreinigungen, und das Experiment ist missglückt.

Die aus dem Wachsthum der Tuberkelbacillen hervorgehenden Culturen erscheinen dem unbewaffneten Auge zuerst in der zweiten Woche nach der Aussaat, gewöhnlich erst nach dem zehnten Tage, als sehr kleine Pünktchen und trocken aussehende Schüppchen, welche, je nachdem die Tuberkelmasse bei der Aussaat mehr oder weniger zerquetscht und durch reibende Bewegungen mit einer grösseren Fläche des Nährbodens in Berührung gebracht wurde, das ausgelegte Tuberkelstückchen in geringerem oder weiterem Umkreise umlagern. Wenn sich nur sehr wenige Bacillen in dem Aussaatmaterial befanden, dann gelingt es kaum, die Bacillen aus dem Gewebe frei zu machen und unmittelbar auf den Nährboden zu bringen, in diesem Falle entwickeln sich inre Colonien im Innern des ausgelegten Gewebstückchens und man sieht, wenn dasselbe transparent genug (p. 225) ist, z. B. in Stückchen, welche scrophulösen Drüsen entnommen sind, bei durchfallendem Licht dunklere, bei auffallendem Licht dagegen weisslich erscheinende Punkte auftreten. Mit Hülfe einer schwachen, ungefähr 30 bis 40 fachen Vergrösserung sind die Bacillencolonien schon gegen Ende der ersten Woche wahrzunehmen. Sie erscheinen als sehr zierliche, spindelförmige und meistens S förmige, aber auch in anderen ähnlichen Figuren gekrümmte Gebilde, welche, wenn sie am Deckglas ausgebreitet, gefärbt und mit starken Vergrösserungen untersucht werden, nur aus den bekannten äusserst feinen

Bacillen bestehen. Bis zu einem gewissen Grade schreitet im Laufe von drei bis vier Wochen das Wachsthum dieser Colonien fort, sie vergrössern sich zu platten, den Umfang eines Mohnkornes meistens nicht erreichenden, schuppenartigen Stückchen, welche dem Nährboden lose aufliegen, niemals selbstständig in denselben eindringen, oder ihn verflüssigen. Die Colonie der Bacillen bildet ausserdem eine so compacte Masse, dass das kleine Schüppchen von dem starren Blutserum mit einem Platindraht im Zusammenhang leicht abgehoben und nur unter Anwendung eines gewissen Druckes zerbröckelt werden kann. Das überaus langsame Wachsthum, welches nur bei Bruttemperatur zu erreichen ist, die eigenthümliche schuppenartige trockene und feste Beschaffenheit dieser Bacillencolonien findet sich bei keiner anderen bis jetzt bekannten Bacterienart wieder, so dass eine Verwechselung der Culturen von Tuberkelbacillen mit denjenigen anderer Bacterien unmöglich und schon bei nur geringer Uebung nichts leichter ist, als zufällige Verunreinigungen der Culturen sofort zu erkennen. Das Wachsthum der Colonien ist, wie gesagt, nach einigen Wochen beendet und eine weitere Vergrösserung tritt wahrscheinlich aus dem Grunde nicht ein, weil die Bacillen jeder Eigenbewegung entbehren und nur durch den Wachsthumprocess selbst auf dem Nährboden verschoben werden, was bei der langsamen Vermehrung der Bacillen natürlich nur in sehr geringen Dimensionen erfolgen kann. Um nun eine solche Cultur im Gange zu erhalten, muss sie einige Zeit nach der ersten Aussaat, ungefähr nach 10 bis 14 Tagen auf einen neuen Nährboden übertragen werden. Dies geschieht so, dass einige Schüppchen mit dem geglühten Platindraht abgenommen und in ein frisches mit sterilisirtem, erstarrten Blutserum versehenes Reagensglas übertragen, daselbst auf dem Nährboden zerdrückt und möglichst ausgebreitet werden. Es entstehen dann in dem gleichen Zeitraum wieder schuppenartige, trockene Massen, welche zusammenfliessen und je nach der Ausdehnung der Aussaat einen mehr oder weniger grossen Theil der Blutserumfläche überziehen. In dieser Weise werden die Culturen fortgesetzt.

Die Tuberkelbacillen lassen sich auch noch auf anderen

Nährsubstraten kultiviren, wenn letztere ähnliche Eigenschaften wie das erstarrte Blutserum besitzen. So wachsen sie beispielsweise auf einer mit Agar-Agar bereiteten, bei Brutwärme hart bleibenden Gallerte, welche einen Zusatz von Fleischinfus und Pepton erhalten hat. Doch bilden sie auf diesem Nährboden nur unförmliche kleine Brocken, niemals so charakteristische Vegetationen, wie auf dem Blutserum.

Ursprünglich habe ich die Tuberkelbacillen nur aus den Lungentuberkeln von Meerschweinchen kultivirt, die mit tuberculösen Substanzen inficirt waren. Die aus verschiedenen Quellen abstammenden Culturen hatten also eine Art Zwischenstufe, den Körper des Meerschweinchens, zu passiren. Hierbei hätte es aber, ebenso wie bei der Uebertragung einer Cultur von einem Reagensglas in ein anderes, leicht zu Irrthümern kommen können, wenn zufällig andere Bakterien mit verimpft wurden oder wenn etwa bei den Versuchsthieren, was gar nicht selten ist, spontane Tuberculose auftritt. Um diese Fehlerquellen zu vermeiden, bedurfte es besonderer Massregeln, welche sich aus den Beobachtungen über das Verhalten der diese Versuche am meisten gefährdenden spontanen Tuberculose ergaben. Unter hunderten von eben angekauften Meerschweinchen, welche gelegentlich anderer Versuche zur Section kamen, habe ich nicht ein einziges tuberculöses gefunden. Die spontane Tuberculose kam immer nur vereinzelt und niemals vor Ablauf von drei bis vier Monaten vor, nachdem die Thiere sich mit tuberculös inficirten in dem nämlichen Raume befunden hatten. Bei Thieren, welche spontan tuberculös erkrankt waren, fanden sich ausnahmslos die Bronchialdrüsen ungemein vergrössert und eitrig geschmolzen, meistens auch in der Lunge ein grosser käsiger Heerd mit weit vorgeschrittenem Zerfall im Centrum, so dass es einige Male ganz wie in menschlichen Lungen zu ächter Cavernenbildung gekommen war. Die Tuberkelentwicklung in den Unterliebsorganen war hinter derjenigen in den Lungen weit zurück. Die Schwellung der Bronchialdrüsen und der Beginn des Processes in den Athmungsorganen lassen keinen Zweifel darüber, dass die spontane Tuberculose dieser Thiere eine Inhalationstuberculose ist, welche aus der Aufnahme

einiger weniger oder möglicherweise nur eines einzelnen Infektionskeimes entstanden ist und deswegen sehr langsam verläuft. Ganz anders verhält sich die Impftuberculose. Die Impfstelle befand sich bei den Thieren am Bauch, in der Nähe der Inguinaldrüsen. Diese schwollen auch zuerst an und gaben damit ein frühes und untrügliches Kennzeichen für das Gelingen der Impfung. Die Tuberculose verlief, weil von vornherein eine grössere Menge des Infektionsstoffes einverleibt wurde, unvergleichlich schneller als die spontane Tuberculose, und bei der Section dieser Thiere wurden die Milz und Leber stärker tuberculös verändert gefunden, als die Lunge. Es ist deswegen durchaus nicht schwierig, die spontane Tuberculose von der Impftuberculose bei den Versuchsthieren zu unterscheiden. Mit Berücksichtigung aller dieser Verhältnisse liess sich wohl annehmen, dass, wenn mehrere eben angekaufte Meerschweinchen in gleicher Weise und mit dem gleichen Material geimpft und von anderen Thieren getrennt in einem besonderen Käfig gehalten wurden, und dann sämmtlich gleichzeitig und schon nach kurzer Frist in der geschilderten, für Impftuberculose charakteristischen Weise erkrankten, dass dann die Entstehung der Tuberculose nur auf die Wirkung der verimpften Substanz zurück zu führen ist.

In der angedeuteten Weise wurde denn auch verfahren und unter allen Cautelen (vorhergehende Desinfection der Impfstelle, Benutzung von kurz vorher geglähten Instrumenten) mit der auf ihre Virulenz zu prüfenden Substanz jedesmal vier bis sechs Meerschweinchen geimpft. Der Erfolg war ein durchweg gleichmässiger; bei sämmtlichen Thieren, welche mit frischen tuberkelbacillenhaltigen Massen geimpft wurden, war die kleine Impfwunde fast immer schon am folgenden Tage verklebt, sie blieb etwa acht Tage lang unverändert, dann bildete sich ein Knötchen, welches sich entweder vergrösserte ohne aufzubrechen oder, was meistens der Fall war, sich in ein flaches trockenes Geschwür verwandelte. Schon nach 2 Wochen waren die auf der Seite der Impfwunde gelegenen Leistendrüsen, bisweilen auch die Achseldrüsen, bis zu Erbsengrösse geschwollen. Von da ab magerten die Thiere schnell ab und starben nach vier bis

sechs Wochen oder wurden, um jede Combination mit etwa später eintretender spontaner Tuberculose auszuschliessen, getödtet. In den Organen aller dieser Thiere, und zwar vorzugsweise in der Milz und Leber, fanden sich die bei Meerschweinchen so sehr charakteristischen, bekannten tuberculösen Veränderungen. Dass in der That bei dieser Versuchsanordnung die Infection der Meerschweinchen nur durch die verimpften Substanzen bewirkt wurde, geht auch noch daraus hervor, dass (p. 226) in mehreren Versuchsreihen mit Impfung einer scrophulösen Drüse, fungöser Massen von einem Gelenk, in welchen beiden Fällen keine Tuberkelbacillen aufgefunden werden konnten, ferner nach Verimpfung von Lungentuberkeln eines Affen, welche 2 Monate lang trocken und mit eben solchen, welche einen Monat lang in Alcohol aufbewahrt gewesen waren, auch nicht ein einziges von den geimpften Thieren erkrankte, während die mit bacillenhaltigen Massen geimpften ausnahmslos vier Wochen nach der Impfung schon hochgradig tuberculös waren.

Von solchen Meerschweinchen, welche durch Impfung mit Tuberkeln aus der Affenlunge, mit Miliartuberkeln aus Gehirn und Lunge vom Menschen, mit käsigen Massen aus phthisischer Lunge, mit Knoten aus den Lungen und vom Peritoneum perlüchtiger Rinder inficirt waren, wurden nun in der früher geschilderten Weise Culturen der Tuberkelbacillen ausgeführt. Es stellte sich heraus, dass ebenso wie das Krankheitsbild, welches die aufgezählten verschiedenen Substanzen beim Meerschweinchen hervorrufen, immer das gleiche ist, so auch die erhaltenen Bacillenculturen sich nicht im Geringsten von einander unterscheiden. Im Ganzen wurden 15 solcher Reinculturen von Tuberkelbacillen gemacht, und zwar 4 von Meerschweinchen, welche mit Affentuberculose inficirt waren, 4 von mit Perlsucht, 7 von mit menschlichen tuberculösen Massen inficirten Meerschweinchen.

Um aber auch jeden Einwand auszuschliessen, dass durch die vorhergehende Verimpfung der tuberculösen Massen auf Meerschweinchen eine Aenderung in der Natur der Bacillen, möglicherweise ein Gleichwerden der bis dahin verschiedenen

Organismen bewirkt sei, wurde versucht, die Tuberkel-Bacillen unmittelbar aus den spontan tuberculös erkrankten Organen von Menschen und Thieren zu cultiviren.

Dieser Versuch gelang mehrfach, und es wurden Reinculturen erhalten aus zwei menschlichen Lungen mit Miliartuberkeln, aus einer eben solchen mit käsiger Pneumonie, zweimal aus dem Inhalt von kleinen Cavernen phthisischer Lungen, einmal aus verkästen Mesenterialdrüsen und zweimal aus frisch exstirpirten scrophulösen Drüsen, ferner zweimal aus perlsüchtiger Rinderlunge und dreimal aus den Lungen von spontan an Tuberculose erkrankten Meerschweinchen. Auch diese Culturen glichen einander vollkommen und ebenso denen, welche auf dem Umwege der Verimpfung auf Meerschweinchen erhalten waren, so dass an der Identität der bei den verschiedenen tuberculösen Processen vorkommenden Bacillen nicht gezweifelt werden kann.

In Bezug auf diese Reinculturen habe ich noch zu erwähnen, dass Klebs, Schüller und Toussaint ebenfalls Microorganismen aus tuberculösen Massen gezüchtet haben. Alle drei Forscher fanden, dass die Culturflüssigkeiten nach der Infection mit Tuberkelstoff schon nach zwei bis drei Tagen sich trübten und zahlreiche Bacterien enthielten. Bei den Versuchen von Klebs traten schnell bewegliche kleine Stäbchen auf, Schüller und Toussaint erhielten Micrococcen. Ich habe mich wiederholt davon überzeugt, dass die Tuberkelbacillen in Flüssigkeiten nur sehr kümmerlich wachsen, dieselben auch niemals trübe machen, weil sie ganz unbeweglich sind, und wenn ein Wachstum stattfindet, dies sich erst im Verlauf von drei bis vier Wochen zu erkennen giebt. Die genannten Forscher müssen es daher mit anderen Organismen als mit den Tuberkelbacillen zu thun gehabt haben.

Bis dahin war durch meine Untersuchungen also festgestellt, dass das Vorkommen von characteristischen Bacillen regelmässig mit Tuberculose verknüpft ist, und dass diese Bacillen sich aus tuberculösen Organen gewinnen und in Reinculturen isoliren lassen. Es blieb nunmehr noch die wichtige Frage zu beantworten, ob die isolirten Bacillen, wenn sie dem Thier-

körper wieder einverleibt werden, den Krankheitsprocess der Tuberculose auch wieder zu erzeugen vermögen.

Um bei der Lösung dieser Frage, in welcher der Schwerpunkt der ganzen Untersuchung über das Tuberkelvirus liegt, jeden Irrthum auszuschliessen, wurden möglichst verschiedene Reihen von Experimenten angestellt, welche wegen der Bedeutung der Sache einzeln aufgezählt werden sollen.

Zunächst wurden Versuche mit einfacher Verimpfung der Bacillen in der früher geschilderten Weise angestellt.

1. Versuch. Von sechs eben angekauften und in einem und demselben Käfig gehaltenen Meerschweinchen wurden vier am Bauch mit Bacillen Cultur geimpft, welche aus menschlichen Lungen mit Miliartuberkeln gewonnen und 54 Tage lang in fünf Umzüchtungen cultivirt waren. Zwei Thiere blieben ungeimpft. Bei den geimpften Thieren schwollen nach 14 Tagen die Inguinaldrüsen, die Impfstellen verwandelten sich in ein Geschwür und die Thiere magerten ab. Nach 32 Tagen starb eines der geimpften Thiere. Nach 35 Tagen wurden die übrigen getödtet. Die geimpften Meerschweinchen, sowohl das spontan gestorbene, als die drei getödteten, wiesen hochgradige Tuberculose der Milz, Leber und Lungen auf; die Inguinaldrüsen waren stark geschwollen und verkäst, die Bronchialdrüsen wenig geschwollen. Die beiden nicht geimpften Thiere zeigten keine Spur von Tuberculose in den Lungen, der Leber oder Milz.

2. Versuch. Von acht Meerschweinchen wurden 6 mit Bacillen-Cultur geimpft, welche aus der tuberculösen Lunge eines Affen abstammend 95 Tage lang in acht Umzüchtungen cultivirt war. Zwei Thiere blieben zur Controle ungeimpft. Der Verlauf war genau derselbe, wie im ersten Versuch. Die 6 geimpften Thiere wurden bei der Section hochgradig tuberculös, die beiden ungeimpften gesund gefunden, als sie nach 32 Tagen getödtet wurden.

3. Versuch. Von 5 Meerschweinchen wurden 5 mit Cultur geimpft, die von perlsüchtiger Lunge herrührte, 72 Tage alt und 6 mal umgezüchtet war. Die 5 geimpften Thiere zeigten sich, als nach 34 Tagen sämmtlich Thiere getödtet wurden, tuberculös, das ungeimpfte gesund.

4. Versuch. Eine Anzahl Thiere (Mäuse, Ratten, Igel, ein Hamster, Tauben, Frösche), über deren Empfänglichkeit für Tuberculose noch nichts bekannt ist, wurden mit Cultur geimpft, welche von tuberculöser Lunge eines Affen gewonnen und 113 Tage lang ausserhalb des Thierkörpers fortgezüchtet war. 4 Feldmäuse, welche 53 Tage nach der Impfung getödtet wurden, hatten zahlreiche Tuberkelknötchen in der Milz, Leber und Lunge, ebenso verhielt sich ein gleichfalls 53 Tage nach der Impfung getödteter Hamster.

In diesen 4 ersten Versuchsreihen hatte die Verimpfung von Bacillen-Culturen am Bauch der Versuchsthiere also eine ganz genau ebenso verlaufende Impftuberculose hervorgebracht, wie wenn frische tuberculöse Substanzen verimpft gewesen wären.

In den nächstfolgenden Versuchen wurde die Impfsubstanz in die vordere Augenkammer von Kaninchen gebracht, um zu erfahren, ob auch bei dem so modificirten Impfverfahren das künstlich cultivirte Tuberkelvirus denselben Effect haben würde, wie das natürliche.

5. Versuch. Drei Kaninchen erhielten ein kleines Bröckchen einer Cultur (von käsiger Pneumonie menschlicher Lunge abstammend und 89 Tage lang fortgezüchtet) in die vordere Augenkammer. Es entwickelte sich schon nach wenigen Tagen eine intensive Iritis, die Hornhaut wurde bald trübe und gelbgrau gefärbt. Die Thiere magerten sehr schnell ab, wurden nach 25 Tagen getödtet und ihre Lungen von zahllosen Tuberkelknötchen durchsetzt gefunden.

(p. 227) 6. Versuch. Von 3 Kaninchen erhält eines eine Injection von reinem Blutserum in die vordere Augenkammer, die beiden anderen eine Injection mit dem nämlichen Blutserum, mit welchem aber einige Bröckchen von einer Cultur (aus Perlsuchtungen abstammend und 91 Tage lang fortgezüchtet) verrieben sind. Bei den beiden letzten Kaninchen traten dieselben Erscheinungen wie im vorigen Versuch ein. Schnell verlaufende Iritis und Trübung der Cornea. Nach 28 Tagen werden die Thiere getödtet. Das erste mit reinem Blutserum injicirte Kaninchen ist vollkommen gesund, die Lungen der beiden

andern Thiere sind mit unzähligen Tuberkelknötchen gleichsam überschüttet.

7. Versuch. Von 4 Kaninchen erhält das erste reines Blutserum in die vordere Augenkammer, dem zweiten wird die Kanüle der Spritze, welche Blutserum mit Zusatz von Bacillen-Cultur (von Affentuberculose abstammend, 132 Tage lang fortgezüchtet) enthält, in die vordere Augenkammer geführt, der Stempel aber nicht bewegt, so dass nur eine minimale Menge der Flüssigkeit in den Humor aq. gelangen kann. Dem 3. und 4. Kaninchen werden von dem mit der Bacillen Cultur versetzten Blutserum mehrere Tropfen in die vordere Augenkammer injicirt. Bei den beiden letzten Thieren entwickelt sich wieder Iritis, Panophthalmitis und es folgt sehr schnelle Abmagerung.

Bei dem zweiten Kaninchen dagegen bleibt das Auge anfangs unverändert, aber im Verlauf der 2. Woche entstehen einzelne weissgelbliche Knötchen auf der Iris in der Nähe der Einstichstelle und es entwickelt sich von da ausgehend eine regelrechte Iristuberculose. Auf der Iris entstehen immer neue Knötchen, sie faltet sich, allmählig trübt sich dann die Cornea und die weiteren Veränderungen entziehen sich der Beobachtung. Nach 30 Tagen werden diese vier Thiere getödtet. Das erste ist vollkommen gesund, beim zweiten finden sich ausser den erwähnten Veränderungen am Auge, die Lymphdrüsen am Kiefer und neben der Ohrwurzel geschwollen und von gelbweissen Herden durchsetzt, die Lungen und übrigen Organe sind noch frei von Tuberculose. Die beiden letzten Kaninchen haben wieder unzählige Tuberkeln in der Lungen.

8. Versuch. 6 Kaninchen werden mit Cultur, welche von menschlicher Lunge mit Miliartuberkeln abstammt und 105 Tage lang fortgezüchtet ist, in derselben Weise wie im vorhergehenden Versuch, das zweite Thier nur durch Einstich in die vordere Augenkammer ohne Injection, inficirt. Es entwickelt sich bei allen 6 Thieren Iristuberculose, bei einigen auch eine über die Nachbarschaft der Impfstelle sich langsam ausbreitende Infiltration der Conjunctiva mit Tuberkelknötchen.

Das Resultat dieser Versuche mit Impfung in die vordere Augenkammer war, wenn möglichst geringe Mengen von Tuber-

kelbacillen eingeführt wurden, ein ganz dem von Cohnheim, Salomonsen und Baumgarten erhaltenen entsprechendes.

Ich begnügte mich damit aber noch nicht, sondern stellte noch fernere Versuche an mit Injection der Bacillen-Culturen in die Bauchhöhle oder direct in den Blutstrom und suchte schliesslich auch noch solche Thiere, deren Infection mit Tuberculose nicht leicht gelingt, durch den künstlich gezüchteten Infektionsstoff tuberculös zu machen.

9. Versuch. Von zwölf Meerschweinchen erhielten zehn Blutserum, welches mit Bacillen Cultur (von Affentuberculose abstammend und 142 Tage gezüchtet) versetzt war, in die Bauchhöhle injicirt. Dem elften wurde reines Blutserum in die Bauchhöhle injicirt und das zwölfte, welches eine ganz frische, bedeutende Bisswunde am Bauche hatte, blieb ohne Einspritzung.

Von den Thieren, welche die Injection erhalten hatten, starben je eins nach 10, 13, 16, 17, 18 Tagen. Die übrigen wurden am 25. Tage nebst den Controlthieren getödtet. Bei den zuerst gestorbenen war das grosse Netz stark verdickt, zusammengeballt und mit einer derben gelblichweissen Masse infiltrirt. Unter dem Microscop stellte sich diese Masse als auszähllosen Tuberkelbacillen bestehend heraus, welche fast sämmtlich mit sehr deutlichen Sporen versehen waren. Die später gestorbenen resp. getödteten Thiere dieser Reihe hatten, ausser der Infiltration des Netzes, bereits Tuberkeleruptionen in Milz und Leber. Die Controlthiere wurden vollkommen gesund befunden.

10. Versuch. Eine Anzahl weisser Ratten war zwei Monate lang fast ausschliesslich mit den Leichen tuberculöser Thiere gefüttert. Von Zeit zu Zeit wurde eine Ratte getödtet und untersucht. Einige Male wurden vereinzelte kleine graue Knötchen in den Lungen dieser Thiere gefunden, die meisten waren ganz gesund geblieben. Auch einfache Impfungen mit tuberculösen Substanzen und mit Culturen aus denselben hatten keinen Effect bei diesen Thieren gehabt, obwohl sie wiederholt versucht wurden. Nachdem die Fütterung mit tuberculösen Massen mehrere Wochen aufgehört hatte, erhielten 5 von diesen Ratten eine Injection mit Bacillen-Cultur (von Affentuberculose und 142 Tage gezüchtet) in die Bauchhöhle. Fünf Wochen

später wurden dieselben getödtet und in den Lungen, sowie in der stark vergrösserten Milz dieser Thiere, zahllose Tuberkelknötchen gefunden. Dieser Versuch ist nicht rein, weil die Fütterung mit tuberculösen Massen vorhergegangen war, aber ich erwähne ihn deshalb, weil es gelungen war, bei Ratten, welche allen Infectionsstoffen gegenüber sich mindestens ebenso resistent verhalten wie Hunde, durch die Injection der Bacillenculturen eine regelrechte Tuberculose zu erzeugen.

11. Versuch. Von 12 Kaninchen erhielten 2 einen halben Ccm. reinen Blutserums in die Ohrvene injicirt. 4 Kaninchen erhielten in derselben Weise Blutserum mit Cultur (von Affentuberculose abstammend und 178 Tage fortgezüchtet), 3 Kaninchen Blutserum mit Cultur (aus menschlicher phthisischer Lunge abstammend und 103 Tage fortgezüchtet) und die 3 letzten Blutserum mit Cultur (von Perlsuchtungen abstammend und 121 Tage lang gezüchtet). Für jede dieser Gruppen wurde eine besondere Spritze benutzt. Die beiden ersten Kaninchen blieben munter und kräftig, alle übrigen magerten rapide ab und fingen schon in der zweiten Woche an schwer zu athmen. Nach 18 Tagen stirbt das erste Thier (Einspritzung mit Cultur phthisischer Lunge), nach 19 Tagen das zweite und dritte (beide hatten Einspritzungen mit Cultur von Affentuberculose erhalten), nach 21 Tagen das vierte (Einspritzung mit Cultur von Perlsucht), nach 25 Tagen das fünfte (mit Cultur von Phthisis inficirt), nach 26 und 27 Tagen das sechste und siebente (mit Cultur von Affentuberculose inficirt), am 30 und 31. Tage zwei weitere Thiere. Das letzte und die beiden Controlthiere wurden am 38. Tage nach der Injection getödtet.

In dem Verhalten der Lunge und der übrigen Organe der mit verschiedenen Culturen inficirten Thiere konnte kein Unterschied wahrgenommen werden. Bei sämmtlichen Thieren fanden sich zahllose Miliartuberkel in den Lungen. Auch die Leber und die Milz von allen diesen Thieren enthielten ausserordentlich viele Tuberkel, doch waren dieselben bei den zuerst gestorbenen nur mikroskopisch klein; bei den später gestorbenen hatten sie sich schon so weit entwickelt, dass sie macroscopisch sichtbar wurden und bei einem Kaninchen zeigten sich auch im

Netz, im Zwerchfell und im Mesenterium viele mit blossen Auge erkennbare Miliartuberkel. Die beiden Controlthiere wurden bei der Section ohne jede Tuberkelablagerung in irgend einem Organ gefunden.

12. Versuch. Zwei ausgewachsene kräftige Katzen erhielten (p. 228) eine Injection in die Bauchhöhle mit Blutserum, welches mit Cultur (von Affentuberkulose erhalten und 162 Tage lang fortgezüchtet) verrieben war. Die eine starb nach 19 Tagen. Das Netz war mit einer derben weisslichen Masse infiltrirt und stellen-weise über einen Centimeter dick. Der seröse Ueberzug der Därme und das Peritoneum hatten ihren Glanz verloren, die Milz war stark vergrössert. Die Infiltration des Netzes bestand ebenso wie bei den Meerschweinchen, welche eine Injection mit Bacillenkultur in die Bauchhöhle erhalten hatten, aus dichten, grösstentheils in Zellen eingebetteten Massen von Tuberkelbacillen. Zu einer makroskopisch erkennbaren Tuberkeleruption war es noch nicht gekommen; aber microscopisch liessen sich zahllose Tuberkel in Lunge, Leber und Milz nachweisen. Die zweite Katze wurde nach 43 Tagen getödtet und es fanden sich bei derselben sehr zahlreiche hirsekorn-grosse Tuberkelknötchen in den Lungen, Milz und Netz, verhältnissmässig wenige in der Leber.

13. Versuch. Einer mehrere Jahre alten Hündin wurden zwei Cubikcentimeter Blutserum, welchem Cultur (von menschlicher Miliartuberkulose abstammend und 94 Tage fortgezüchtet) beigemischt war, in die Bauchhöhle injicirt. In den ersten beiden Wochen nach der Injection war an dem Thiere keine Veränderung zu bemerken, dann verlor es an Munterkeit, frass weniger und vom Ende der dritten Woche an zeigte sich eine deutliche Auftreibung des Leibes. Zu Anfang der fünften Woche wurde es getödtet. In der Bauchhöhle befand sich ein ziemlich reichlicher Erguss einer klaren, schwachgelblichen Flüssigkeit. Das Netz, Mesenterium und Mutterbänder waren mit sehr vielen Tuberkelknötchen besetzt, ebenso die Oberfläche des Darms und der Blase. Die vergrösserte Milz, die Leber und Lungen enthielten Zahllose Miliartuberkel. Von den Injectionsstellen war

nichts mehr zu erkennen und nirgends eine Spur von käsigem Eiter.

Es bedarf wohl kaum der Erwähnung, dass die zu allen diesen Versuchen benutzten Spritzen vor jedem Gebrauch durch einstündiges Erhitzen auf 160 bis 170° C. sicher desinficirt waren.

Vielfach wurden die Tuberkelknötchen, welche sowohl durch Impfung als durch Injection mit den Bacillenkulturen erhalten waren mikroskopisch untersucht und vollkommen identisch gefunden mit den gewöhnlichen spontan oder nach Impfung mit tuberkulösen Massen bei diesen Thieren entstandenen Tuberkeln. Sie hatten ganz dieselbe Anordnung der zelligen Elemente und waren auch vielfach mit Riesenzellen versehen, welche ebenso wie diejenigen der spontanen Tuberkel Bacillen einschlossen. Ferner wurden aus den Tuberkeln, welche vermittelt der Bacillenculturen erhalten waren, von neuem die Bacillen in Reinculturen isolirt und mit diesen sowohl als mit den Tuberkeln Impfversuche angestellt, welche ganz dasselbe Resultat wie Impfungen mit menschlichen Tuberkeln oder Perlsuchtlinge ergaben. Also auch in dieser Beziehung verhielten sich die durch Infection mit Culturen erhaltenen Tuberkel wie die natürlich vorkommenden.

Blickt man auf diese Versuche zurück, so ergibt sich, dass eine nicht geringe Zahl von Versuchsthieren, denen die Bacillenculturen in sehr verschiedener Weise, nämlich durch einfache Impfung in das subcutane Zellgewebe, durch Injection in die Bauchhöhle oder in die vordere Augenkammer, oder direct in den Blutstrom beigebracht waren, ohne nur eine Ausnahme tuberculös geworden waren und zwar hatten sich bei ihnen nicht etwa einzelne Knötchen gebildet, sondern es entsprach die ausserordentliche Menge der Tuberkel der grossen Zahl der eingeführten Infectionskeime. An anderen Thieren war es gelungen durch Impfung möglichst geringer Mengen von Bacillen in die vordere Augenkammer ganz dieselbe tuberkulöse Iritis zu erzeugen, wie sie in den bekannten für die Frage der Impftuberculose ausschlaggebenden Versuchen von Cohnheim, Salomonsen und Baumgarten nur durch ächte tuberkulöse Substanz erhalten war.

Eine Verwechslung mit spontaner Tuberkulose oder eine zufällige unbeabsichtigte Infection der Versuchsthiere mit Tuberkel-Virus ist in diesen Experimenten aus folgenden Gründen ausgeschlossen. Erstens kann weder die spontane Tuberkulose noch eine zufällige Infection in einem so kurzen Zeitraum diese massenhafte Eruption von Tuberkeln veranlassen. Zweitens blieben die Controlthiere, welche genau in derselben Weise wie die inficirten Thiere behandelt wurden, nur mit dem einzigen Unterschied, dass sie keine Bacillencultur erhielten, gesund. Drittens kam bei zahlreichen zu andern Versuchszwecken in derselben Weise mit anderen Substanzen geimpften und injicirten Meerschweinchen und Kaninchen niemals dieses typische Bild von Miliartuberkulose vor, welches nur dann entstehen kann, wenn der Körper auf einmal mit einer grossen Menge von Infectionskeimen gewissermassen überschüttet wird.

Alle diese Thatsachen zusammengenommen berechtigen zu dem Ausspruch, dass die in den tuberculösen Substanzen vorkommenden Bacillen nicht nur Begleiter des tuberculösen Processes, sondern die Ursache desselben sind, und dass wir in den Bacillen das eigentliche Tuberkelvirus vor uns haben.

Damit ist auch die Möglichkeit gegeben, die Grenzen der unter Tuberculose zu verstehenden Krankheit zu ziehen, was bisher nicht mit Sicherheit geschehen konnte. Es fehlte an einem bestimmten Kriterium für die Tuberculose, und der Eine rechnete dazu Miliartuberculose, Phthisis, Scrophulose, Perlsucht u. s. w., ein Anderer hielt vielleicht mit ebenso viel Recht alle diese Krankheitsprocesse für different. In Zukunft wird es nicht schwierig sein zu entscheiden, was tuberculös und was nicht tuberculös ist. Nicht der eigenthümliche Bau des Tuberkels, nicht seine Gefässlosigkeit, nicht das Vorhandensein von Riesenzellen wird den Ausschlag geben, sondern der Nachweis der Tuberkelbacillen, sei es im Gewebe durch Farbenreaction, sei es durch Cultur auf erstarrtem Blutserum. Dies Kriterium als das massgebende angenommen, müssen nach meinen Untersuchungen Miliartuberculose, käsige Pneumonie, käsige Bronchitis, Darm- und Drüsentuberculose, Perlsucht des Rindes, spontane und Impftuberculose bei Thieren für identisch

erklärt werden. Ueber Scrophulose und fungöse Gelenkaffectionen sind meine Untersuchungen zu wenig zahlreich, um ein Urtheil zu ermöglichen. Jedenfalls gehört ein grosser Theil der scrophulösen Drüsen- und Gelenkleiden zur ächten Tuberculose. Vielleicht sind sie ganz mit der Tuberculose zu vereinigen. Der Nachweis von Tuberkelbacillen in den verkästen Drüsen eines Schweines, in den Tuberkelknötchen eines Huhnes lässt vermuthen, dass die Tuberculose auch unter den Hausthieren eine grössere Verbreitung hat, als gemeinhin angenommen wird und es ist sehr wünschenswerth auch nach dieser Richtung hin das Verbreitungsgebiet der Tuberculose genau kennen zu lernen.

Nachdem die parasitische Natur der Tuberculose somit festgestellt ist, müssen zur Vervollständigung der Aetiologie noch die Fragen beantwortet werden, woher die Parasiten stammen und wie sie in den Körper gelangen.

In Bezug auf die erste Frage ist es nothwendig zu entscheiden, ob der Infectionsstoff nur unter Verhältnissen, wie sie im thierischen Körper gegeben sind, sich entwickeln, oder ob er, wie z. B. die Milzbrandbacillen auch unabhängig vom thierischen Organismus an irgend welchen Stellen in der freien Natur seinen Entwicklungsgang durchmachen kann.

(p. 229) Es ergab sich nun in mehreren Versuchen, dass die Tuberkelbacillen nur bei Temperaturen zwischen 30 und 41° C. wachsen. Unter 30° fand ebenso wie bei 42° innerhalb drei Wochen nicht das geringste Wachsthum statt, während beispielsweise Milzbrandbacillen noch bei 20° und zwischen 42° und 43° C. kräftig wachsen. Schon auf Grund dieser einen Thatsache kann die aufgestellte Frage entschieden werden. Im gemässigten Klima ist ausserhalb des Thierkörpers keine Gelegenheit für eine mindestens 2 Wochen anhaltende gleichmässige Temperatur von über 30° C. geboten. Es folgt daraus, dass die Tuberkelbacillen in ihrem Entwicklungsgang lediglich auf den thierischen Organismus angewiesen, also nicht gelegentliche, sondern ächte Parasiten sind, und nur aus dem thierischen Organismus stammen können.

Auch die zweite Frage, wie die Parasiten in den Körper ge-

langen, ist zu beantworten. Die weit überwiegende Mehrzahl aller Fälle von Tuberculose nimmt ihren Anfang in den Respirationswegen und der Infectionsstoff macht sich zuerst in den Lungen oder in den Bronchialdrüsen bemerklich. Es ist also hiernach sehr wahrscheinlich, dass die Tuberkelbacillen gewöhnlich mit der Athemluft, an Staubpartikelchen haftend, eingeathmet werden. Ueber die Art und Weise, wie dieselben in die Luft kommen, kann man wohl nicht in Zweifel sein, wenn man erwägt, in welchen Unmassen die im Caverneninhalte vorhandenen Tuberkelbacillen von Phthisikern mit dem Sputum ausgeworfen und überall hin verschleppt werden.

Um über das Vorkommen der Tuberkelbacillen im phthisischen Sputum eine Anschauung zu gewinnen, habe ich wiederholt die Sputa von einer grossen Reihe von Phthisikern untersucht und gefunden, dass in manchen derselben keine, aber ungefähr in der Hälfte der Fälle ganz ausserordentlich zahlreiche Bacillen, darunter auch sporenhaltige, vorhanden waren. Nur beiläufig sei bemerkt, dass in einer Anzahl Proben von Sputum nicht phthisisch Kranker die Tuberkelbacillen niemals gefunden wurden. Mit solchem frischen bacillenhaltigen Sputum geimpfte Thiere wurden ebenso sicher tuberculös, als wie nach Impfung mit Miliartuberkeln.

Aber auch nach dem Eintrocknen verloren derartige infectiöse Sputa ihre Virulenz nicht. So wurden vier Meerschweinchen durch Impfung mit zwei Wochen altem, trockenen Sputum, ferner vier Meerschweinchen durch Impfung mit vier Wochen lang trocken aufbewahrtem Sputum und weitere vier Meerschweinchen durch acht Wochen hindurch trocken gehaltenes Sputum ganz in derselben Weise tuberculös, wie nach Infection mit frischem Material. Demnach lässt sich wohl annehmen, dass das am Boden, Kleidern u. s. w. eingetrocknete phthisische Sputum längere Zeit seine Virulenz bewahrt und, wenn es verstäubt in die Lungen gelangt, daselbst Tuberculose erzeugen kann. Vermuthlich wird die Haltbarkeit der Virulenz von der Sporenbildung der Tuberkelbacillen abhängen und es ist in dieser Beziehung wohl zu berücksichtigen, dass die Sporen-

bildung, wie wir an einigen Beispielen gesehen haben, bereits im thierischen Organismus selbst und nicht wie bei den Milzbrandbacillen ausserhalb desselben vor sich geht.

Auf die Verhältnisse der erworbenen oder ererbten Disposition, welche in der Aetiologie der Tuberculose unzweifelhaft eine bedeutende Rolle spielen, jetzt schon eingehen zu wollen, würde zu sehr in das Gebiet der Hypothese führen. Nach dieser Richtung hin bedarf es noch eingehender Untersuchungen, ehe ein Urtheil gestattet ist. Nur auf einen Punkt, welcher zur Erklärung mancher räthselhaften Erscheinungen dienen kann, möchte ich aufmerksam machen; das ist das überaus langsame Wachsthum der Tuberkelbacillen. Dasselbe bewirkt höchst wahrscheinlich, dass die Bacillen nicht, wie beispielsweise die ungemein schnell wachsenden Milzbrandbacillen, von jeder beliebigen kleinen Verletzung des Körpers aus zu inficiren vermögen. Wenn man ein Thier mit Sicherheit tuberculös machen will, dann muss der Infectionsstoff in das subcutane Gewebe, in die Bauchhöhle, in die vordere Augenkammer, kurz an einen Ort gebracht werden, wo die Bacillen Gelegenheit haben, sich in geschützter Lage vermehren und Fuss fassen zu können. Infectionen von flachen Hautwunden aus, welche nicht in das subcutane Gewebe dringen, oder von der Cornea gelingen nur ausnahmsweise. Die Bacillen werden wieder eliminirt, ehe sie sich einnisten können.

Hieraus erklärt sich, weshalb die Sectionen von tuberculösen Leichen nicht zur Infection führen, auch wenn kleine Schnittwunden an den Händen mit tuberculösen Massen in Berührung kommen. Kleine schwache Hautschnitte sind eben keine für das Eindringen der Bacillen geeigneten Impfwunden. Aehnliche Bedingungen werden sich auch für das Haften der in die Lungen gerathenen Bacillen geltend machen. Es werden wahrscheinlich besondere, das Einnisten der Bacillen begünstigende Momente, wie stagnirendes Secret, Entblössung der Schleimhaut vom schützenden Epithel u. s. w., zu Hülfe kommen müssen, um die Infection zu ermöglichen. Es wäre sonst kaum zu verstehen, dass die Tuberculose, mit der wohl jeder Mensch, namentlich

an dicht bevölkerten Orten, mehr oder weniger in Berührung kommt, nicht noch häufiger inficirt, als es in Wirklichkeit geschieht.

Fragen wir nun danach, welche weitere Bedeutung den bei der Untersuchung der Tuberculose erhaltenen Resultaten zukommt, so ist es zunächst als ein Gewinn für die Wissenschaft anzusehen, dass es zum ersten Male gelungen ist, den vollen Beweis für die parasitische Natur einer menschlichen Infectiouskrankheit, und zwar der wichtigsten von allen vollständig zu liefern. Bisher war dieser Beweis nur für Milzbrand erbracht, während von einer Anzahl den Menschen betreffenden Infectiouskrankheiten z. B. von Recurrens, von den Wundinfectiouskrankheiten, Lepra, Gonorrhoe nur das gleichzeitige Vorkommen der Parasiten mit dem pathologischen Process bekannt war, ohne dass das ursächliche Verhältniss zwischen diesen beiden erwiesen werden konnte. Es lässt sich erwarten, dass die Aufklärungen, welche über die Aetiologie der Tuberculose gewonnen sind, auch für die Beurtheilung der übrigen Infectiouskrankheiten neue Gesichtspunkte ergeben, und dass die Untersuchungsmethoden, welche sich bei der Erforschung der Tuberculose-Aetiologie bewährt haben, auch bei der Bearbeitung anderer Infectiouskrankheiten von Nutzen sein werden. Ganz besonders möchte dies letztere für Untersuchungen über diejenigen Krankheiten gelten, welche wie Syphilis und Rotz mit der Tuberculose am nächsten verwandt sind und mit ihr zusammen die Gruppe der Infectious-Geschwulstkrankheiten bilden.

In wie weit die Pathologie und Chirurgie die Kenntnisse über die Eigenschaften der Tuberculose-Parasiten verwerthen können, ob beispielsweise der Nachweis der Tuberkelbacillen im Sputum zu diagnostischen Zwecken benutzt werden kann, ob die sichere Bestimmung mancher local-tuberculöser Affectionen auf die chirurgische Behandlung derselben von Einfluss sein wird, und ob nicht möglicher Weise auch die Therapie aus weiteren Erfahrungen über die Lebensbedingungen der Tuberkelbacillen Nutzen ziehen kann, das alles zu beurtheilen, ist nicht meine Aufgabe.

Meine Untersuchungen habe ich im Interesse der Gesund-

heutspfege vorgenommen, und dieser wird auch, wie ich hoffe, der grösste Nutzen daraus erwachsen.

(p. 230) Bisher war man gewöhnt, die Tuberculose als den Ausdruck des socialen Elends anzusehen und hoffte von dessen Besserung auch eine Abnahme dieser Krankheit. Eigentliche gegen die Tuberculose selbst gerichtete Massnahmen kennt deswegen die Gesundheitspflege noch nicht. Aber in Zukunft wird man es im Kampf gegen diese schreckliche Plage des Menschengeschlechtes nicht mehr mit einem unbestimmten Etwas, sondern mit einem fassbaren Parasiten zu thun haben, dessen Lebensbedingungen zum grössten Theil bekannt sind und noch weiter erforscht werden können. Der Umstand, dass dieser Parasit nur im thierischen Körper seine Existenzbedingungen findet und nicht, wie die Milzbrandbacillen, auch ausserhalb desselben unter den gewöhnlichen natürlichen Verhältnissen gedeihen kann, gewährt besonders günstige Aussichten auf Erfolg in der Bekämpfung der Tuberculose. Es müssen vor allen Dingen die Quellen, aus denen der Infectionsstoff fliesst, so weit es in menschlicher Macht liegt, verschlossen werden. Eine dieser Quellen und gewiss die hauptsächliche ist das Sputum der Phthisiker, um dessen Verbleib und Ueberführung in einen unschädlichen Zustand bis jetzt nicht genügend Sorge getragen ist. Es kann nicht mit grossen Schwierigkeiten verknüpft sein, durch passende Desinfectionsverfahren das phthisische Sputum unschädlich zu machen und damit den grössten Theil des tuberculösen Infectionsstoffes zu beseitigen. Gewiss verdient daneben auch die Desinfection der Kleider, Betten u. s. w., welche von Tuberculösen benutzt wurden, Beachtung.

Eine andere Quelle der Infection mit Tuberculose bildet unzweifelhaft die Tuberculose der Hausthiere, in erster Linie die Perlsucht. Damit ist auch die Stellung gekennzeichnet, welche die Gesundheitspflege in Zukunft der Frage nach der Schädlichkeit des Fleisches und der Milch von perlsüchtigen Thieren einzunehmen hat. Die Perlsucht ist identisch mit der Tuberculose des Menschen und also eine auf diesen übertragbare Krankheit. Sie ist deswegen ebenso wie andere vom Thier auf den Menschen übertragbare Infectionskrankheiten zu be-

handeln. Mag nun die Gefahr, welche aus dem Genuss von perlsüchtigem Fleisch oder Milch resultirt, noch so gross oder noch so klein sein, vorhanden ist sie und muss deswegen vermieden werden. Es ist hinlänglich bekannt, dass milzbrandiges Fleisch von vielen Personen und oft lange Zeit hindurch, ohne jeden Nachtheil genossen ist, und doch wird Niemand daraus den Schluss ziehen, dass der Verkehr mit solchem Fleisch zu gestatten sei.

In Bezug auf die Milch perlsüchtiger Kühe ist es bemerkenswerth, dass das Uebergreifen des tuberculösen Processes auf die Milchdrüse von Thierärzten nicht selten beobachtet ist, und es ist deswegen wohl möglich, dass sich in solchen Fällen das Tuberkelvirus der Milch unmittelbar beimischen kann.

Es liessen sich noch eine Anzahl weiterer Gesichtspunkte über Massregeln aufstellen, welche auf Grund unserer jetzigen Kenntnisse über die Aetiologie der Tuberculose zur Einschränkung dieser Krankheit dienen könnten, doch würde eine Besprechung derselben hier zu weit führen. Wenn sich die Ueberzeugung, dass die Tuberculose eine exquisite Infectiouskrankheit ist, unter den Aerzten Bahn gebrochen haben wird, dann werden die Fragen nach der zweckmässigsten Bekämpfung der Tuberculose gewiss einer Discussion unterzogen werden und sich von selbst entwickeln.



The Etiology of Tuberculosis

BY

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VILLEMIN's discovery that tuberculosis is transmissible to animals has found varied confirmation, as is well known, but also apparently well founded opposition, so that, up to a few years ago, it remained undecided as to whether or not tuberculosis is an infectious disease. Since then, however, the inoculations into the anterior chamber of the eye, carried out first by Cohnheim and Salomonsen and later by Baumgarten, and, in addition, the inhalation experiments of Tappeiner and others have proven the transmissibility of tuberculosis beyond a doubt, and, in the future, it must be awarded a place among the infectious diseases.

If the number of victims which a disease claims is taken as a measure of its importance, then all diseases, especially the most feared contagious diseases, plague, cholera, etc., must take a place far behind that of tuberculosis. Statistics show that 1/7 of all people die of tuberculosis, and if only the productive middle aged class is considered, tuberculosis carries away a third and often more of these. Thus the public health has cause enough for devoting its attention to such a fatal disease, wholly aside from the fact that still other conditions, of which only the re-

lationship between human and bovine tuberculosis need be mentioned, lay a claim to the interest of hygiene.

Since it now becomes the task of the health officials to make the infectious diseases the object of investigation from the standpoint of public health, and thus primarily of etiology, it now appears as a pressing duty to conduct penetrating investigations particularly of tuberculosis.

Attempts have been made repeatedly to investigate the nature of tuberculosis thoroughly, but up to now they have been fruitless. The so frequently successful staining methods used for the demonstration of pathogenic microorganisms have left this disease in the lurch, and the attempts made to isolate and cultivate the virus of tuberculosis up to the present can not be regarded as successful; so that Cohnheim in the recently published latest edition of his lectures in general pathology had to speak of "the direct demonstration of the virus of tuberculosis as a yet unsolved problem".

In my investigations of tuberculosis, I at first followed the known methods without obtaining any explanation as to the true nature of the disease. However, several opportune observations caused me to abandon these methods and to adopt others which finally led me to positive results.

The aim of the investigations had to be directed first toward the demonstration of some sort of parasitic organism foreign to the body, which possibly could be explained as the cause of the disease. This demonstration was indeed carried out successfully by means of a certain staining method, with the aid of which characteristic bacteria, previously unknown, were found in all organs affected by tuberculosis. It would take too long to describe the manner in which I arrived at this new procedure and therefore I shall pass at once to its description.

The material to be examined is prepared in the usual manner for examining for pathogenic bacteria, and either spread on the cover slip, dried and heated or cut into sections after fixation in alcohol. The cover slips or sections are placed in a staining solution of the following constitution: 200 c.c. of distilled water are mixed with 1 c.c. of a concentrated alcoholic solution of methyl-

ene blue, shaken up, and then 0.2 c.c. of a 10% solution of potassium hydroxide is added with repeated shaking. This mixture must show no precipitate after standing for several days. The materials to be stained remain in this solution for 20 to 24 hours. By heating the solution to 40°C. in a water bath this time can be shortened to $\frac{1}{2}$ to 1 hour. Following this the cover slips are covered with a concentrated aqueous solution of vesuvin which is filtered each time before using, and after 1 to 2 minutes rinsed with distilled water. When the cover slips come from the methylene blue, the attached layer appears dark blue and is markedly (p. 222) overstained. During the treatment with vesuvin this blue color is lost and it appears stained a faint brown. Under the microscope all the constituents of animal tissue, that is, the cell nuclei and their products of disintegration appear brown, while the tubercle bacilli, on the other hand, stain a beautiful blue. Moreover, all other bacteria which I have investigated to date, with the exception of the lepra bacilli, take on a brown color with this staining method. The color contrast between the brown stained tissue and the blue tubercle bacilli is so striking that the latter, which are present often only in very small number, nevertheless, are to be found and identified with the greatest certainty.

Sections are treated in an entirely similar manner. They are transferred from the methylene blue to the filtered vesuvin solution, remain there from 15 to 20 minutes and are then rinsed in distilled water until the blue color has disappeared and a more or less intense brown tint is left. Following this they are dehydrated with alcohol, cleared in oil-of-cloves and can be examined microscopically at once in this fluid or else finally embedded in Canada balsam. In these preparations also the tissue constituents are stained brown and the tubercle bacilli a vivid blue.

Moreover, the bacteria are not stained only by methylene blue, but with the simultaneous operation of alkalies, take up other anilin dyes with the exception of the brown dyes; the staining, however, is not nearly as beautiful as that with methylene blue. Furthermore, in the staining process described, the potassium solution can be replaced by sodium or ammonia, from which

it can be concluded that the potassium itself does not play an essential role, but it is only the strong alkalinity of the solution that matters. The fact that the bacteria can be stained by a stronger addition of the potassium in places where they no longer come to view with a solution containing less potassium is further confirmation of this. However, the tissues of the cut sections shrink and change so much under the influence of stronger potassium solutions that the latter are only exceptionally of value.

The bacteria made visible by this method show a behavior which, in many respects, is characteristic. They have a rod shaped form and thus belong to the group of bacilli. They are very thin and are from a quarter to one-half of the diameter of a red blood corpuscle in length; however, at times they attain greater length, up to the full diameter of a red blood cell. In shape and size they bear a striking similarity to the lepra bacilli; yet they differ from the latter in that they appear a little slimmer and pointed at the ends. Also with Weigert's nuclear staining method, the lepra bacilli take up the stain, which the tubercle bacilli do not do. The bacilli are present in large numbers in all situations where the tuberculous process is early in origin and making rapid progress; they then usually form little groups which are pressed closely together and at times are arranged in bundles. Many times these lie within cells and present a picture like that of lepra bacilli heaped within the cells. On the other hand, many free bacilli are found. Particularly on the borders of large caseous foci, crowds of bacilli which are not inclosed in cells are found.

As soon as the height of the tuberculous process is passed the bacilli become more rare, are found only in small groups or entirely alone on the edges of tuberculous foci, along with weakly stained and at times scarcely recognizable bacilli, which are dying or already dead. Finally, they may disappear completely, yet they are rarely entirely absent and then only in those cases in which the tuberculous process is arrested.

If giant cells are present in the tuberculous tissue, then the bacilli lie chiefly within these structures. In very slowly progressing tuberculous processes the interior of the giant cells is usually the only place in which the bacilli are to be found. In

this case the majority of giant cells contain only one or a few bacilli; and it makes a surprising impression to continually meet new groups of giant cells in wide stretches of the cut section, which contain one or two tiny blue rods suspended almost in the center in the wide space surrounded by the brown stained nuclei. Often the bacilli are seen in only small numbers of giant cells, at times only solitary specimens are met, while at the same time many other giant cells are free of them. In this case those containing the bacilli are the younger ones as judged from their size and position, the bacilli free, on the other hand, are the older ones; and from this it can be assumed that the latter originally contained bacilli, that these have died or passed over into the resting state, which is soon to be mentioned. According to analogy with the formation of giant cells about foreign bodies, such as vegetable fibers and *Strongylus* eggs, as observed by Weiss, Friedlander and Laulamie, one can conceive of the relationship between the giant cells and bacilli as follows; that the bacilli, as foreign bodies, have been engulfed by the giant cells and thus if the giant cell is empty and all other signs indicate a tuberculous process, the probability is that it previously harbored one or more bacilli and that these have given cause to its origin.

In addition, the bacilli may be observed unstained in the unprepared condition. For this it is necessary to examine carefully and in a hanging drop, in order to avoid streaming of the fluid, a little material taken from locations which contain a significant number of bacilli, for example from a gray tubercle of a lung of a guinea pig dead of inoculation tuberculosis. Then the bacilli appear as very fine rods, which show only molecular movements but have not the slightest motility of their own.

Under certain conditions, to be mentioned later, the bacilli form spores, even in the animal body; and indeed, the single bacillus contains several, usually 2 to 4, spores of oval form which are distributed throughout its length.

In regard to the presence of the bacilli in the various tuberculous processes in man and animals the following material has been observed.

1) Human. 11 cases of miliary tuberculosis. The bacilli were

never lacking in the miliary tubercles in the lungs; often, however, in nodules the centers of which no longer took up the nuclear stain, bacilli were not to be found; but here they were present, even in greater numbers, at the edge of the tubercle and in younger tubercles not yet caseous at the center. (p. 223) Beside the lungs they could be demonstrated in miliary tubercles of the spleen, liver and kidneys. They were present in abundance in the gray nodules of the pia mater in basilar meningitis. Also, in several cases examined, the caseous bronchial glands contained, in part, dense swarms of bacilli many of which bore spores, and in part, a few bacilli in the interior of giant cells and in the center of tubercles embedded in the lymphoid tissue and composed of epithelioid cells surrounded by giant cells.

12 cases of caseous bronchitis and pneumonia (cavity formation in six cases). The presence of the bacilli was limited chiefly to the edges of the caseous, infiltrated tissues, but they were frequently very abundant. Occasionally nests of bacilli are encountered in the infiltrated portions of the lungs. In most cavities the bacilli are uncommonly numerous. The well known tiny caseous particles in the contents of the cavities consist almost entirely of masses of bacilli. Among the bacilli present in the soft caseous foci and in the cavities, numbers bearing spores were encountered at times. In large cavities they are present mixed with other bacteria, but easily differentiated from them because, as described in the method of staining, only the tubercle bacilli take the blue tint, while the other bacteria, as already mentioned, stain brown.

1 case of solitary tubercle of the brain, larger than a hazel nut. The caseous mass of the tubercle was surrounded by cellular tissue in which many giant cells were embedded. The majority of giant cells contained no parasites, but occasionally groups of giant cell each containing one or two bacilli were met.

2 cases of intestinal tuberculosis. In the tubercles grouped about the intestinal ulcers, the bacilli could be demonstrated especially well, and indeed, here again they were found particularly numerous in the most recent and smallest nodules. In addition,

the bacilli were present in large numbers in the mesenteric lymph nodes of both these cases.

3 cases of recently excised scrofulous lymph nodes. In only two of these could bacilli inclosed in giant cells be demonstrated.

4 cases of proliferative arthritis. In two cases bacilli were found but only in small isolated groups of giant cells.

II) In animals. 10 cases of bovine tuberculosis with calcified nodules in the lungs, several also in the peritoneum, and, in one case, on the pericardium. In all cases the bacilli were present, principally within the giant cells which were in the tissue surrounding the calcified masses. The distribution of the bacilli is so uniform that among numerous giant cells, scarcely one is to be found that does not contain one or more bacilli, sometimes as many as twenty. In one of these cases, the bacilli also could be demonstrated in the bronchial lymph nodes, and in a second, in the mesenteric nodes.

3 cases in which the lungs of cattle did not contain the usual calcified nodules with uneven surfaces of the usual tuberculosis, but on the contrary, smooth walled, round nodules filled with thick, soupy, cheesy material. Usually this form is not regarded as tuberculosis, but as bronchiectasis. However, in the vicinity of these nodules, giant cells were found and in them the tubercle bacilli.

One caseous cervical lymph node of a pig contained the bacilli.

In the organs of a fowl dead of tuberculosis, and, indeed, in tubercles of the bone marrow, as well as in the peculiar nodules of the intestines, liver and lungs, large numbers of bacilli were found.

In three monkeys, spontaneously dead of tuberculosis, the lungs, spleen, liver, omentum, which were riddled with countless nodules, and the caseous lymph nodes, were examined and tubercle bacilli found in all the nodules or in their immediate vicinity.

Of spontaneously ill animals, nine guinea pigs and seven rabbits came to examination, which disclosed the bacilli everywhere in the tubercles.

Beside these cases of spontaneous tuberculosis, there was provided for me a not inconsiderable number of animals which were

infected by means of inoculation with various tuberculous substances; that is, with gray and caseous tubercles from human beings, with sputum from consumptives, with tuberculous material from spontaneously afflicted monkeys, rabbits and guinea pigs, with material from various lungs of cattle with bovine tuberculosis, calcified as well as caseous, and finally from tuberculous affections obtained by sub-inoculations. The number of animals infected in this way amounts to 172 guinea pigs, 32 rabbits and 5 cats. The demonstration of the bacilli in the majority of these cases had to be limited to examination of the tubercles of the lungs which were always present in large numbers. In these the bacilli were not absent a single time; often they were extraordinarily numerous, at times spore bearing, only a few definitely recognizable specimens occasionally being found in the preparations.

It is striking that in spite of the regularity of the occurrence of the tubercle bacilli, no one up to the present has seen them. Yet this can be explained by the fact that the bacilli are extraordinarily tiny structures and for the most part are so scant in number, especially when their presence is limited to the interior of the giant cells, that without special staining methods they must escape the most careful observer. Even though they are present in large numbers, they are mixed with finely granular detritus and obscured by it in such a way that their recognition is extremely difficult.

Moreover, there are several accounts of micro-organisms having been found in tissues showing the changes of tuberculosis. Thus Schüller mentions in his paper on scrofulous and tuberculous joint diseases that he has found micrococci constantly. Doubtless we are concerned here, just as in the case of Klebs, who found extremely tiny motile granules in tubercles, with something other than the tubercle bacilli which I observed, and which are non-motile and rod shaped. Also Aufrecht, as he states in the first volume of his pathological reports, has found, in the center of tubercles of three rabbits out of a number which he infected with tuberculous and bovine tuberculous material, short rod-like structures along with two different types of micrococci.

The long axes of the former measured about half the length of the transverse diameter. The tubercle bacilli, however, are at least five times as long as they are thick, often much longer in comparison to their thickness; furthermore, in uncomplicated tuberculosis, they never occur mixed with micrococci or other bacteria in the tubercle. It is therefore most unlikely that Aulfrecht has seen the true (p. 224) tubercle bacillus. If this were the case, then he should have been able to demonstrate it in human and bovine tuberculous lungs and the striking relationship between the tubercle bacilli and the giant cells could not have escaped him.

On the basis of my numerous observations I state it to be proved that the bacteria designated by me as the tubercle bacilli are present in all cases of tuberculous disease of man and animals, and that they may be differentiated from all other microorganisms by their characteristic properties. It does not necessarily follow from this coincidence of the tuberculous disease and the bacilli that the two phenomena have an original association, although no small amount of probability is given to this theory by the fact the bacilli are found chiefly where the process is beginning or progressing, and that they disappear in those places where the disease comes to a standstill.

In order to prove that tuberculosis is a parasitic disease caused by the invasion of the bacilli and primarily influenced by the growth and proliferation of the latter, the bacilli had to be isolated from the body and cultivated in pure culture until devoid of all adherent products of disease originating from the animal organism; and, finally, through transfer of the isolated bacilli to animals, the same clinical picture of tuberculosis as is obtained empirically by the injection of naturally developed tuberculous material had to be produced.

Omitting the many preliminary investigations which led to the solution of this problem, here again only the finished method will be described. Its principle depends on the use of a solid, transparent culture medium which retains its firm consistency at incubator temperature. I have described at length the advantage of this method of obtaining pure cultures, which I have intro-

duced into the study of bacteria, in an earlier publication. That the solution of the complicated problem of cultivating the tubercle bacilli in pure culture has been reached by means of the same method, is to me an additional proof of the efficiency of this method.

Serum of cattle or sheep blood, which is obtained as purely as possible, is poured into cotton stoppered test tubes and daily, for six consecutive days, is heated to a temperature of 58°C . for an hour at a time. By this means it is possible to sterilize the serum completely in most instances, although not always, when everything else may fail. Then it is heated to 65°C . for several hours, indeed, until it has become coagulated and firm. After this treatment, the serum appears as amber yellow, completely transparent or at least only slightly opalescent, firm, gelatinous material; and does not show the slightest development of bacterial colonies if it is left for many days at incubator temperature. In order to obtain a large surface for the laying out of cultures the serum is allowed to become fixed with the test tubes slanted as much as possible. For such cultures as are to be made directly accessible to microscopic investigation the serum is placed in flat watch glasses or hollow glass blocks for hardening.

On this solidified blood serum, which forms a firm transparent culture medium at incubator temperature, the tuberculous material is placed in the following manner:—

The simplest way, in which the experiment almost without exception succeeds, presents when an animal just dead of tuberculosis or one killed for this purpose is used. First the skin is deflected over the breast and thorax with instruments just previously flamed. With a flamed pincers and clippers the ribs are then cut in the middle and the anterior wall of the chest is removed without entering the abdominal cavity, so that the lungs lie free throughout a large extent. The instruments are now replaced by other freshly disinfected ones, single tubercles or particles of one of the size of a millet seed are excised from the lung tissue quickly with the scissors and at once transferred to the surface of the solidified blood serum in the test tube, by means of a just previously flamed platinum wire fused into a glass rod. Nat-

usually the cotton plug is removed for only the shortest possible time. In this manner a number of test tubes, about six or ten, are treated with tuberculous material, because, in spite of the most cautious manipulation, not all of the tubes remain free of accidental contamination.

Lymph glands, in which there is beginning caseation, lend themselves to this experiment just as well as the pulmonary tubercles; less well, on the other hand, the pus from broken down glands, which usually contains very few or almost no bacilli.

The direct culture of bacilli from tuberculous human organs or from the lungs of bovine tuberculosis is more difficult. I have washed objects of this sort, the removal of which from the body I was not able to care for with the previously mentioned precautions, carefully and repeatedly with bichloride of mercury, then removed the surface layers with flamed instruments and taken the material for inoculation from the deep portions where it is to be expected that contaminating bacteria were not yet able to penetrate.

The test tubes, treated in the described manner with tuberculous material, are placed in the incubator and must remain there constantly at a temperature from 37° to 38°C . In the first week no noteworthy changes are observed. If one should occur and if rapidly growing bacterial proliferation takes place in the first few days, spreading out from the material inoculated or indeed at a distance from it, which usually is recognized by white, gray or yellow drops, often with liquefaction of the blood serum, then we are dealing with a contaminant and the experiment has miscarried.

The cultures resulting from the growth of tubercle bacilli first appear to the naked eye in the second week after inoculation, usually not until after the tenth day, as very tiny points and dry scales, which, according to whether the tuberculous material is more or less broken up during inoculation and brought into contact with a larger surface of the culture medium by means of rubbing motions, lie about the fragments of the tubercles in tiny or wide areas. If only a very few bacilli were present in the material inoculated, then it is hardly ever possible to free the bacilli

from the tissue and bring them into direct contact with the culture medium. In this case they develop their colonies within the bits of tissue and if this is transparent enough, (p. 225) if, for example, it is in small pieces which have been taken from scrofulous glands, whitish, shining points may be seen within it when the light strikes it. By the aid of low magnification, approximately 30 to 40 times, the colonies may be perceived by the end of the first week. They appear as very fine, spindle shaped, usually S shaped or similarly bent structures, which, when spread out on a cover glass, stained and examined under high magnification, consist only of the exceedingly fine bacilli described. The growth of the colonies progresses up to a certain extent during the course of three to four weeks, as they enlarge to flat scale like bits, which usually do not reach the size of a poppy seed in circumference, and which lie loosely on the surface of the culture medium and never penetrate it spontaneously or liquefy it. The colony of bacilli, furthermore, forms such a compact mass that the little scale can be raised easily from the solidified blood serum with a platinum wire and can be broken up only by the exertion of a certain amount of pressure. The markedly slow growth which is attained only at incubator temperature, the peculiarly dry and scale like condition of these bacillary colonies occur in no other known type of bacteria, so that confusion of the cultures of tubercle bacilli with those of other bacteria is impossible; and after only a small amount of practice nothing is easier to detect at once than accidental contamination of the cultures. The growth of the colonies ceases after several weeks, as has been said already, and further enlargement probably does not occur because the bacilli are lacking in motility and are forced out on the culture medium only through the growth process itself, which, because of the slow proliferation of the bacilli, naturally can proceed only in very short dimensions. In order to keep such a culture going, it must be transplanted to new culture material at some time after the first inoculation, approximately after 10 to 14 days. This is done by taking several scales on a flamed platinum wire and placing them in a fresh test tube containing sterilized, solidified blood serum, crushing them on

the culture medium and spreading them out as far as possible. Then, after the same time interval, scale-like, dry masses spring up, which coalesce and cover more or less of the surface of the blood serum, according to the extent of their inoculation. In this manner the culture is carried on.

The tubercle bacilli also can be cultivated on other culture media which have properties similar to that of the blood serum. Thus, for example, they will grow on a jelly which remains firm at incubator temperature, and is prepared from agar-agar containing an infusion of meat and peptone. However, on this medium, they form only shapeless small flecks and never the characteristic vegetations as on the blood serum.

Originally I cultivated tubercle bacilli only from the pulmonary tubercles of guinea pigs which had been infected with tuberculous material. Thus the cultures originating from various sources had to pass through a sort of intermediary state, that is, in the body of the guinea pig. But in this also, as in the transfer of a culture from one test tube to another, mistakes could occur easily, if, by chance, other bacteria were also injected or if spontaneous tuberculosis were present in the laboratory animals, as is not seldom the case. To avoid these sources of error, special precautions were necessary; these being obtained by observations of spontaneous tuberculosis, which is most dangerous to this experiment. Among hundreds of recently bought guinea pigs, which opportunely came to autopsy in the course of other experiments, I have never found a single tuberculous one. Spontaneous tuberculosis always occurred in isolated instances and never before the course of 3 to 4 months during which time the animals had been in the same room with those infected with tuberculosis. In animals spontaneously ill of tuberculosis, I found the bronchial lymph nodes, without exception, to be uncommonly large and broken down into pus and usually in the lungs also a large caseous focus with far advanced necrosis in the center, so that several times true cavity formation had taken place exactly as in human lungs. The development of tubercles in the abdominal viscera lagged far behind that in the lungs. The swelling of the bronchial lymph nodes and the beginning of the process in the respira-

tory apparatus leaves no doubt that the spontaneous tuberculosis of these animals is an inhalation tuberculosis, which arises from the taking up of only a few or possibly only a single germ and which then progresses very slowly. Inoculation tuberculosis acts in an entirely different manner. The site of inoculation in these animals was in the belly in the vicinity of the inguinal lymph nodes. These swelled first of all and thereby gave an early and infallible sign as to the success of the inoculation. The tuberculosis ran a much more rapid course than the spontaneous tuberculosis, because to begin with, a larger amount of infectious material was taken into the body; and on section of these animals, the spleen and liver showed far more changes of tuberculosis than did the lungs. Thus it is not at all difficult to differentiate spontaneous tuberculosis from inoculation tuberculosis in laboratory animals. Bearing these considerations in mind, if a number of newly bought guinea pigs were inoculated at the same time and with the same material and kept segregated from other animals in a special cage, and then, simultaneously, after a short space of time, all became ill in the characteristic manner described for inoculation tuberculosis, it can be assumed that the origin of the tuberculosis was to be attributed only to the effects of the material injected.

In the manner described and taking all precautions (previous disinfection of the site of inoculation, use of previously flamed instruments), four to six guinea pigs were inoculated each time with the material to be tested for virulence. The results were uniform throughout. In all animals which were inoculated with fresh material containing tubercle bacilli the tiny injection wound was almost always crusted over on the following day. It remained unchanged for about 8 days, then a nodule formed which either enlarged without breaking down or, as was the usual case, developed into a flat dry ulcer. Within two weeks the inguinal nodes on the side of the inoculation wound, at times also the axillary nodes, were enlarged to pea size. From then on the animals quickly became emaciated, and died after 4 to 6 weeks, or were killed in order to avoid any combination with a later developing spontaneous tuberculosis. In the organs of all these

animals, and chiefly in the spleen and liver, the characteristic, well known tuberculous changes of guinea pigs were found. That, indeed, the infection of the guinea pigs in this series of experiments resulted only from the injected material is demonstrated by the fact that, (p. 226) in other series of experiments with inoculation of a scrofulous gland, and fungous material from a joint in which no tubercle bacilli could be found, and after injections of pulmonary tubercles (monkey), which had been dried for two months and with some which had been kept in alcohol for a month, *not a single one of the animals inoculated became ill*, while those injected with material containing bacilli showed marked tuberculosis in four weeks without exception.

From such guinea pigs as had been infected by inoculation with tubercles from the lungs of monkeys, with miliary tubercles from the brain and lungs of humans, with caseous material from phthisical lungs and with nodes from the lungs and peritoneum of tuberculous cattle, cultures of tubercle bacilli were obtained in the manner previously described. As a result, it was found that, just as the clinical picture which the various substances enumerated produced in the guinea pigs never varied, so the cultures of bacilli obtained did not differ from one another in the slightest degree. In all, fifteen such pure cultures of tubercle bacilli were obtained and of these four were from guinea pigs which were infected with tuberculosis from monkeys, four with bovine tuberculosis and seven with tuberculous material from humans.

However, in order to exclude any possible objection that a change in the nature of the bacilli, possibly a bringing about of similarity between previously dissimilar organisms, was caused by the inoculation of the tuberculous material into the guinea pigs, an attempt was made to cultivate the tubercle bacilli directly from the spontaneously diseased organs of humans and animals.

This experiment succeeded many times and pure cultures were obtained from two human lungs with miliary tuberculosis, from another with caseous pneumonia, twice from the contents of small cavities of phthisical lungs, once from caseous mesenteric nodes and twice from freshly extirpated scrofulous nodes, in

addition, twice from the lungs of cattle with bovine tuberculosis and three times from the lungs of guinea pigs spontaneously ill of tuberculosis. Moreover, these cultures were entirely similar to one another, just as were those obtained by the round-about method of inoculating guinea pigs, so that the unity of identity of the bacilli present in the various tuberculous processes can not be doubted.

In regard to these pure cultures, I must mention that Klebs, Schüller and Toussaint have also cultured microorganisms from tuberculous material. All three investigators found that the culture fluids became cloudy and contained numerous bacteria two or three days after inoculation with tuberculous material. In Klebs' experiments little motile rods were soon present, Schüller and Toussaint obtained micrococci. I have convinced myself repeatedly that tubercle bacilli grow only sparsely in liquids and never render it turbid, because they are entirely non-motile and, if growth occurs, it takes three to four weeks to become recognizable. The investigators mentioned, therefore, must have been working with organisms other than the tubercle bacilli.

Thus, up to this point, my investigations have established that the presence of characteristic bacilli is regularly bound up with tuberculosis and that these bacilli can be obtained from tuberculous organs and isolated in pure culture. It now remained to answer the weighty question as to whether the isolated bacilli if again introduced into the body, are able to produce the pathological processes of tuberculosis.

In order to exclude any error from the solution of this question, wherein lies the crux of the whole investigation of the tubercle virus, series of experiments, as varied as possible, were set up and shall be enumerated in detail because of the significance of the point in question.

First, experiments with simple inoculation of the bacilli in the manner previously described were set up.

Experiment 1. Of six newly bought guinea pigs which were kept in the same cage, four were inoculated on the abdomen with cultures of bacilli obtained from human lungs with miliary

tuberculosis and cultivated for 54 days through five changes of culture material. Two animals remained uninjected. After 14 days the inguinal nodes of the inoculated animals swelled, the sites of injection ulcerated and the animals became emaciated. After 32 days one of the animals inoculated died. After 35 days the remainder of the animals were killed. The injected animals, the one which had died as well as the three which were killed, showed advanced tuberculosis of the spleen, liver and lungs; the inguinal nodes were greatly swollen and caseous, the bronchial nodes but slightly swollen. Neither of the animals which were not injected showed the slightest trace of tuberculosis in the lungs, the liver or the spleen.

Experiment 2. Of 8 guinea pigs, 6 were inoculated with cultures of bacilli which originated from the tuberculous lungs of monkeys and were cultivated for 95 days with eight transfers. Two animals remained uninjected for controls. The course was exactly the same as in the first experiment. The six injected animals showed advanced tuberculosis at autopsy; the two uninjected ones were found healthy when they were killed after 32 days.

Experiment 3. Of 6 guinea pigs, 5 were inoculated with cultures arising from a lung of bovine tuberculosis, 72 days old, transferred six times. The 5 injected animals were found tuberculous, the uninjected ones healthy, after 34 days when all the animals were killed.

Experiment 4. A number of animals (mice, rats, hedge-hogs, a hamster, pigeons, frogs) whose susceptibility to tuberculosis is not known, were inoculated with cultures obtained from the tuberculous lung of a monkey and cultivated for 113 days outside of the animal body. Four field mice, killed 53 days after injection, had numerous tubercles in the spleen, liver and lungs, as did the hamster, killed 53 days after inoculation.

In these first four experiments the inoculation of cultures of bacilli on the abdomen of the experimental animals has thus produced the same clinical picture of tuberculosis as when fresh tuberculous material had been injected.

In the following experiments the material inoculated was

placed in the anterior chamber of the eye of rabbits in order to learn, by this means of inoculation also, whether the artificially cultivated tubercle virus had the same effect as the natural one.

Experiment 5. Three rabbits received a tiny fragment of a culture (obtained from caseous pneumonia of a human lung and grown for 89 days) in the anterior chamber of the eye. After a few days an intensive iritis developed, the cornea soon became cloudy and yellowish gray in color. The animals quickly became emaciated, were killed after 25 days and their lungs found riddled with countless tubercles.

(p. 227) Experiment 6. Of 3 rabbits, one received an injection of pure blood serum in the anterior chamber of the eye, the other two an injection with the same blood serum with which a bit of a culture (from a lung of bovine tuberculosis carried for 91 days) had been mixed. In the latter two rabbits the same phenomena occurred as in the previous experiment. Iritis running a rapid course and haziness of the cornea. After 28 days the animals were killed. The first rabbit, injected with pure blood serum, was completely well, the lungs of both other animals were riddled with countless tubercles.

Experiment 7. Of 4 rabbits, the first received pure blood serum in the anterior chamber. The cannula of the syringe which contained serum, to which a culture of bacilli (from an ape with tuberculosis, cultivated for 132 days) was added, was introduced into the anterior chamber of the second, but the plunger was not moved, so that only a minimal amount of the fluid could reach the aqueous humor. In the 3rd and 4th rabbits several drops of serum with the culture of bacilli were injected into the anterior chamber. In both the last two rabbits, iritis and panophthalmitis again developed and emaciation quickly followed.

On the other hand, in the second rabbit, the eye at first remained unchanged, but in the course of the second week a few yellowish white nodules developed on the iris in the vicinity of the point of injection and from these a typical tuberculous iritis developed. New nodules continually developed on the iris, it became wrinkled, the cornea then gradually became hazy

and obscured the further changes from observation. After 30 days these four animals were killed. The first was completely well, in the second, beside the changes mentioned in the eye, the lymph glands along the jaw and next to the root of the ear were found to be swollen and studded with yellowish white foci; the lungs and remaining organs were, as yet, free from tuberculosis. The last two rabbits as usual had numerous tubercles in the lungs.

Experiment 8. Six rabbits were infected in the same manner as the second animal in the preceding experiment with a culture which originated from a human lung with miliary tuberculosis and which was cultivated for 105 days, receiving only a needle prick in the anterior chamber without injection. Tuberculosis of the iris developed in all 6 animals; in some also a slowly developing infiltration of the conjunctiva with tubercles in the region of the site of injection.

The result of these experiments of inoculation into the anterior chamber of the eye, when only the smallest possible amount of tubercle bacilli are introduced, was wholly in accord with those of Cohnheim, Salmonsens, and Baumgarten.

I did not content myself with this alone, but set up still further experiments with injections of cultures of bacilli into the abdominal cavity or directly into the blood stream, and finally sought to render such animals tuberculous with artificially cultivated virus as are not easily infected.

Experiment 9. Of twelve guinea pigs, ten received blood serum, to which was added a culture of bacilli (originating from monkey tuberculosis and cultivated for 142 days) injected into the peritoneal cavity. Pure blood serum was injected into the peritoneal cavity of the eleventh, while the twelfth, which had a fresh bite on the abdomen of some significance, remained uninjected.

Of the animals injected, one died after 10, 13, 16, 17 and 18 days. The remainder were killed on the 25th day along with the control animals. In the first to die the great omentum was markedly thickened, matted together and infiltrated with thick yellowish white masses. Under the microscope, these masses

were seen to consist of countless tubercle bacilli, almost all of which contained very definite spores. The animals which died later, as well as those which were killed, had tuberculous eruptions in the spleen and liver, in addition to the infiltration of the omentum. The control animals were found to be completely healthy.

Experiment 10. A number of white rats were fed for two months almost exclusively on the bodies of tuberculous animals. From time to time a rat was killed and examined. Several times small, solitary, gray nodules were found in the lungs of these animals which, for the most part, remained healthy. Also, simple inoculations of these animals with tuberculous materials and cultures of the same had no effect, although they were tried repeatedly. After the feeding with tuberculous material had been stopped for several weeks, five of these rats received intraperitoneal injections with a culture of bacilli (from simian tuberculosis, cultivated for 142 days). Five weeks later they were killed and numerous tubercles were found in the lungs, as well as in the greatly enlarged spleens of these animals. This experiment is not pure, because the feeding with tuberculous material had preceded, but I mention it because it was successful in producing typical tuberculosis, by injection of cultures of bacilli, in rats, which are only slightly less resistant to all infectious material than dogs.

Experiment 11. Of 12 rabbits, 2 received 0.5 cc. of pure blood serum in the ear vein. Four rabbits received in the same manner, blood serum with a culture (originating from tuberculosis of monkeys and cultivated for 178 days); 3 rabbits blood serum with culture (from phthisical human lungs, cultivated for 103 days); and the 3 last, blood serum with culture (from a lung of bovine tuberculosis, cultured 121 days). A separate syringe was used for each of these groups. The first two rabbits remained active and well, all the others rapidly became emaciated and during the second week, began to breathe with difficulty. The first animal died after 18 days (injected with culture from phthisical lung); after 19 days, the second and third (both had received injections with cultures of simian tuberculosis); after

21 days the fourth (injected with culture of bovine tuberculosis); after 25 days, the fifth (injected with a culture from pulmonary tuberculosis); after 26 and 27 days, the sixth and seventh (injected with culture of simian tuberculosis) and on the 30th and 31st days, two other animals. The last and the two controls were killed on the 38th day after the injection.

No difference in the contents of the lungs and other organs could be made out among the animals infected with the different cultures. In all animals countless miliary tubercles were found in the lungs. Also the livers and the spleens of all these animals contained extraordinarily many tubercles, yet these were only of microscopic size in those first to die, in those dying later they had developed so far that they were visible macroscopically, and in one rabbit miliary tubercles recognizable to the naked eye were also visible in the omentum, in the diaphragm and in the mesentery. The two controls were found to be without tuberculous deposits anywhere in their organs.

Experiment 12. Two strong, full grown cats each received (p. 228) an injection in the peritoneal cavity of blood serum which was mixed with a culture (of simian tuberculosis, cultured for 162 days). One died after 19 days. The omentum was infiltrated with thick white material and in some places was over a centimeter in thickness. The serous surfaces of the intestines and the peritoneum had lost their sheen, the spleen was markedly enlarged. The infiltration of the omentum, as in the guinea pigs that had received intraperitoneal injections of cultures of bacilli, consisted of thick masses of tubercle bacilli, for the most part, embedded in cells. Although it had not yet progressed to a macroscopically recognizable tuberculous eruption, countless tubercles could be demonstrated microscopically in the lungs, liver and spleen. The second cat was killed after 43 days and in this numerous tubercles, the size of millet seeds, were found in the lungs, spleen and omentum, comparatively few in the liver.

Experiment 13. A bitch several years old was injected intraperitoneally with two cc. of blood serum with which a culture (from human miliary tuberculosis and grown for 94 days) had been mixed. In the first two weeks after injection no changes

were to be observed in the animal, then its spirit was lost, it ate less and from the end of the third week on, it showed definite distension of the abdomen. At the beginning of the fifth week it was killed. A fairly abundant extravasation of clear, pale yellow fluid was found in the peritoneal cavity. The omentum, mesentery and broad ligaments contained many tubercles as did the surfaces of the intestines and bladder. The enlarged spleen, the liver and lungs contained countless miliary tubercles. The site of injection could not be recognized and nowhere was there a trace of caseous pus.

It hardly needs be mentioned that the syringes used in all these experiments were disinfected by an hour's heating between 160 and 170°C. each time before using.

The tubercles obtained by inoculation, as well as by injection of the cultures of bacilli, were examined microscopically many times and found to be completely identical with the usual spontaneous tubercles or those resulting from the inoculation of tuberculous material into these animals. They had entirely the same arrangement of the cellular elements, and very often contained giant cells which held tubercle bacilli just as those in the spontaneous tubercles. In addition, the bacilli were freshly isolated in pure culture from the tubercles obtained by means of the cultures, and inoculation experiments were set up with these as well as with the tubercles, all yielding the same results as inoculation with human or bovine tuberculosis. In this regard, the tubercles resulting from infection with cultures were similar to those occurring naturally.

If one looks back over these experiments, it is apparent that a not inconsiderable number of experimental animals that had received the cultures of bacilli in various ways, that is, by simple inoculation into the subcutaneous tissue, through injection into the abdominal cavity, or into the anterior chamber of the eye or directly into the blood stream, had been rendered tuberculous without a single exception; and, indeed, had not developed only a solitary tubercle but the extraordinary number of tubercles was proportionate to the large number of infectious germs introduced. In other animals it was possible by the injection of a

minimal number of bacilli into the anterior chamber of the eye, to produce a tuberculous iritis, as had been done in the well known experiments of Cohnheim, Salomonsen and Baumgarten so vital in regard to the question of the inoculation of tuberculosis only by true tuberculous material.

A confusion with spontaneous tuberculosis or an accidental unintentional infection of the experimental animals in these experiments is excluded on the following grounds. First of all, neither spontaneous tuberculosis nor an accidental infection can cause this massive eruption of tubercles in so short a space of time. Secondly, the control animals which were treated in exactly the same manner as the infected animals, with the single difference, that they received no culture of bacilli, remained healthy. Thirdly, this typical picture of miliary tuberculosis never occurred in numerous guinea pigs and rabbits injected and infected in the same way with other substances for other experimental purposes, as it then only arises when the body is overcome to a certain extent by a large amount of infectious germs at one time.

All these facts, taken together, substantiate the claim that the bacilli present in tuberculous material, not only accompany the tuberculous process, but are actually the cause of it, and that, in these bacilli, we have the true virus of tuberculosis.

Thus it is also made possible to delimit what diseases shall be understood as tuberculosis, which up to now could not be done with certainty. A definite criterion for tuberculosis was lacking and one person included miliary tuberculosis, phthisis, scrofula, bovine tuberculosis, etc., while another, perhaps just as correctly, regarded all these processes as different. In the future it will not be difficult to decide what is tuberculous and what is not. Not the peculiar structure of the tubercles, not the presence of giant cells, will settle the question, but the demonstration of tubercle bacilli, whether it be in the tissues by the staining reactions or whether it be by culture on solidified blood serum. Accepting this criterion as standard, miliary tuberculosis, caseous pneumonia, caseous bronchitis, intestinal and glandular tuberculosis, bovine tuberculosis and spontaneous and inoculation

tuberculosis in animals must be declared identical as the result of my investigations. In regard to scrofula and proliferative joint affections, my investigations have not been sufficiently numerous to render judgment. At any rate, a large part of the scrofulous glands and joint diseases are truly tuberculous. Perhaps they are all to be considered one with tuberculosis. The demonstration of tubercle bacilli in the caseous lymph nodes of a pig, and in the tubercles of a hen, allows us to assume that tuberculosis has a much larger incidence among the domestic animals than is generally accepted, and this is worth knowing in order that we may learn to know the incidence of tuberculosis in general.

Having established the parasitic nature of tuberculosis, it must be determined from whence the parasites come and how they gain entrance to the body, in order to answer completely the question as to etiology.

In regard to the first question, it is necessary to discover whether the infectious material will develop only under the conditions existing in the animal body, or whether it can develop in any stage free in nature, as, for example, the anthrax bacillus is independent of the animal organism.

(p. 229) It was now determined by many experiments that the tubercle bacilli grow only in temperatures between 30° and 41°C . Below 30° , just as at 42° , the slightest growth did not occur within three weeks, while anthrax bacilli, for example, grow vigorously even at 20° and between 42° and 43°C . On the basis of this one fact, the questions raised can be decided. In the temperate climate, with the exception of the animal body, no opportunity is offered for a uniform temperature of over 30°C . of at least two weeks duration. From this it follows, that the tubercle bacilli must turn to the animal organism exclusively in their developmental processes; thus, they are not occasional parasites but true parasites and can arise only from the animal organism.

The second question as to how the parasites enter the body is also answered. The vast majority of all cases of tuberculosis have their origin in the respiratory passages and the infectious material first makes itself manifest in the lungs or in the bronchial

nodes. Thus it is also highly probable that the tubercle bacilli are usually inhaled with the inspired air, clinging to particles of dust. There can be no doubt as to the manner in which they reach the air if one considers in what large quantities the tubercle bacilli, present in the contents of cavities of patients with pulmonary tuberculosis, must be expectorated with the sputum and thus spread all about.

In order to gain some idea as to the presence of tubercle bacilli in the sputum of phthisical patients, I have examined repeatedly the sputa from a large series of patients with pulmonary tuberculosis and have found that in many of them none is present, but in about half the cases, they are extraordinarily numerous, some of them containing spores. As a corollary, it was noted that, in a number of tests of patients not having phthisis, the tubercle bacilli were never found. Animals injected with this fresh sputum containing bacilli became tuberculous just as surely as after inoculation with miliary tubercles.

Also, when dry, infectious sputa of this sort do not lose their virulence. Thus, by injection of two weeks old dried sputum, four guinea pigs were rendered tuberculous, in the same way as after infection with fresh material, as were four guinea pigs with sputum kept dry for four weeks and also four more by sputum kept dry for eight weeks. Accordingly, it can be assumed easily that on the floor, clothes, etc., dried phthisical sputum retains its virulence for a long time and if it reaches the lungs in the form of dust, it can produce tuberculosis. Possibly the retention of virulence is dependent on the spore formation of the tubercle bacilli, and it is well to recall in this respect that spore formation, of which we have seen several examples, takes place within the animal organism itself, and not outside of it, as is the case with the anthrax bacilli.

At present, it would lead us too far into the realm of hypothesis to go into the condition of the acquired or inherited predisposition, which undoubtedly plays a significant rôle in the etiology of tuberculosis. In this respect, more penetrating investigation is necessary before judgment can be made. I should like to draw attention to only one point which can serve to explain

many puzzling phenomena and that is the extremely slow growth of the tubercle bacilli. This is very likely the reason that the bacilli are not able to infect each and every little wound of the body, as are the uncommonly rapidly growing anthrax bacilli, for example. If one wishes to infect an animal with certainty, then the infectious material must be placed in the subcutaneous tissue, the peritoneal cavity, or the anterior chamber of the eye, in short, in some location where the bacilli are able to reproduce in a protected position and to gain a foothold. Infections of superficial skin wounds, which do not penetrate into the subcutaneous tissue, or of the cornea, are only occasionally successful. The bacilli are eliminated before they are able to establish themselves.

This explains why autopsies on tuberculous bodies do not lead to infection, even if small cuts on the hands do come into contact with tuberculous material. Little cuts in the skin are not suitable inoculation wounds for the entrance of the bacilli. Similar conditions would also hold in the lungs for the harboring of inhaled bacilli. It is probably necessary for certain favorable conditions for the establishing of the bacilli to hold, such as stagnation of secretions, denudation of the protective epithelium of the mucous membrane, etc., in order to make infection possible. Otherwise it would be difficult to understand why tuberculosis is not much more common than it really is, since every person, especially in the more densely inhabited areas, comes into more or less contact with it.

If we now ask what further significance the results obtained in this investigation of tuberculosis have, then it is to be regarded as a victory for science that it has been successful, for the first time, in furnishing complete proof of the parasitic nature of a human infectious disease; indeed, of the most important one of all. Up to now such proof had been established only for anthrax, while for a number of infectious diseases affecting man, for example, relapsing fever, wound infection, leprosy, gonorrhea, the simultaneous presence of the parasite with the pathologic process was known without being able to prove the causal relationship between the two. It can be expected that the explanation of

the etiology of tuberculosis will produce new points of view for the forming of opinions regarding the other infectious diseases, and that the methods of investigation, which have been used successfully in seeking out the etiology of tuberculosis, will be of use in working out the other infectious diseases. This last may be of special significance for those diseases, which, like syphilis and glanders, are closely related to tuberculosis and, together with it form the group of infectious granulomata.

As to how much the knowledge of the properties of the tuberculosis parasite will be of value to pathology and surgery, if, for example, the demonstration of tubercle bacilli in the sputum can be used for diagnostic purposes, if the certain diagnosis of many local tuberculous infections will have an influence on their surgical treatment, and if in some possible manner therapy can be based on further experiences with the living conditions of the tubercle bacilli, to judge of all these things, is not my task.

I have undertaken my investigations in the interests of public health and from them, I hope, the greatest possible benefit will be derived.

(p. 230) Up to the present it has been customary to regard tuberculosis as an expression of social poverty, and to hope by improvement of this to reduce the disease also. On this account, the public health knew no measures specifically directed against tuberculosis. But in the future, in the battle with this horrible plague of the human race, it will be known that we are no longer dealing with an indefinable Something, but with a definite parasite whose vital processes are, for the most part, known, and which can be studied still further. The fact that this parasite finds its proper living conditions only in the animal body and can not exist in the outside world under the usual natural conditions, as do the anthrax bacilli, promises a favorable outlook in the battle with tuberculosis. Thus before anything else, the sources from which the infectious material flows must be closed as far as is humanly possible. One of these sources, and certainly the greatest, is the sputum of consumptive patients, the disposal of which and the change into a harmless state of which, up to the present have not received sufficient care. It can not

be reckoned as extremely difficult to render phthisical sputum harmless by disinfection, and thus cut off the greatest part of the infectious tuberculous material. Also, the disinfection of the clothes, beds, etc., which are used by tuberculous patients should receive consideration.

Tuberculosis of domestic animals, especially bovine tuberculosis, undoubtedly forms another source of infection. The position is indicated as to what stand public health should take in the future on the question of the danger of the meat and milk of animals with bovine tuberculosis. Bovine tuberculosis is identical with the tuberculosis of man, and thus it is a disease which is transmissible to man. Therefore, it is to be treated exactly as any other infectious disease of animals which can be carried to man. Thus 'though the danger resulting from the flesh or milk of bovine tuberculosis be great or small, nevertheless it is present and must be avoided. It has long been known that anthrax meat is eaten by many people, and often over a long period of time, without any ill effects, and yet no one would draw the conclusion from this that the trade in such meat should be permitted.

In regard to the milk of tuberculous cows, it is noteworthy that frequently involvement of the mammary glands by the tuberculous process has been observed by veterinarians, and it is therefore easily possible that in such cases the tubercle virus can be mixed directly with the milk.

A number of other points in regard to regulations which, on the basis of our present knowledge of the etiology of tuberculosis, might serve to limit the disease may be mentioned, but a discussion of these would lead too far at the present time. If the conviction that tuberculosis is an exquisite infectious disease makes its way among the doctors, then the question of a purposeful attack on tuberculosis certainly will come under discussion and it will develop of itself.

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SIR BENJAMIN COLLINS BRODIE
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Sir Benjamin Collins Brodie

BIOGRAPHY

- 1783 Born, son of a clergyman, in Winterslow, in Wiltshire, who was descended from a Jacobite exile in England.
- 1801 Age 18. Sent to London to study medicine; attended anatomical lectures given by Abernethy at St. Bartholomew's Hospital and by James Wilson at the Great Windmill Street School of Medicine.
- 1803 Age 20. Pupil of Sir Everard Home, Surgeon to St. George's Hospital.
- 1805 Age 22. House Surgeon at St. George's from May until November, then became assistant to Dr. Home. Lectured at Great Windmill Street until 1812.
- 1808 Age 25. Became assistant surgeon to St. George's Hospital and lectured there until 1840. Influenced by Bichat, at first devoted himself to physiologic experimentation.
- 1809 Age 26. Opened office in Sackville Street.
- 1810 Age 27. Elected Fellow of the Royal Society.
- 1811 Age 28. Won Copley Medal for two papers on influence of nervous system on production of animal heat. Gave the Croonian lecture.
- 1813 Age 30. Described disease of joints now called by his name.
- 1816 Age 33. Married Miss Sellon; three children survived the parents.
- 1819 Age 36. Moved into larger house in better district because of increasing practice. Succeeded William Lawrence as Professor of Comparative Anatomy and

Physiology at The Royal College of Surgeons—held post until 1823.

- 1822 Age 39. Became full Surgeon at St. George's.
- 1828 Age 45. Surgeon to King George IV.
- 1832 Age 49. Serjeant Surgeon to William IV. Described Abscess of Bones, (Brodie's Abscess).
- 1834 Age 51. Became Member of Council of Royal College of Surgeons of England and Member of Court of Examiners because of attendance on King. Raised to rank of Baronet.
- 1840 Age 57. Resigned as Surgeon to St. George's Hospital. Described Sero-Cystic Tumour of Breast, (Brodie's Tumour).
- 1844 Age 61. Elected President of The Royal College of Surgeons, England
- 1858 Age 75. First President of General Medical Council until 1860. President of the Royal Society until 1861. Later suffered from double cataract for which he was operated on by Sir William Bowman.
- 1862 Age 79. October 21, died at his home, Broome Park, Surrey, of a painful disease of the shoulder.

Also: Member of National Association for the Promotion of Social Science.

D. C. L., Oxford.

President of Royal Medical and Chirurgical Society.

Member of Institute of France.

Member of Academy of Medicine of Paris.

Member of Royal Academy of Sciences of Stockholm.

Member of National Institution of Washington.

Brodie's personal appearance is thus described by Mr. Holmes who knew him personally in his latter years:

"Keen grey eyes, a noble and sensitive mouth and facial muscles which followed all the movements of one of the most active of minds, lent to the countenance a charm and an impressiveness to which no stranger could be insensible. His frame was slight

and small; but there was nothing of weakness in it, and its movements were vigorous and even brusque, such as are habitual to a man whose whole life is passed in constant activity."

EPONYMS

1. **ABSCESS:** A chronic inflammation and ulceration, sometimes tuberculous, of bone, especially in the head of the tibia.
2. **BURSA:** Beneath the semimembranous and the inner head of the gastrocnemius muscles.
3. **DISEASE OF JOINTS:** Chronic synovitis, especially of the knee joint, in which the affected parts acquire a soft and putty consistence.
4. **DISEASE OF SPINE:** Hysteric pseudo-fracture.
5. **JOINT:** See knee.
6. **KNEE:** Chronic synovitis of the knee joint.
7. **OPERATION:** For fissure or ulcer of anus, the muscle fibers of the sphincter being divided at one side by a history drawn from the anus laterally outward.
8. **PAIN:** That induced by folding the skin near a joint affected with neuralgia.
9. **PILE:** Sentinel pile—a mass of inflamed and traumatized anal mucosa at the lower end of a fissure-in-ano.
10. **TUMOR:** Serocystic tumor of the breast; cystadenoma or chronic systic mastitis.

BIBLIOGRAPHY OF WRITINGS

A—Army Medical Library.

B—New York State Library.

C—New York Academy of Medicine Library.

D—Kings County Medical Society, Brooklyn, Library.

E—Lane Medical Library of Stanford University.

1. Account of the dissection of a human fetus in which the circulation of the blood was carried on without a heart. Phil. Trans., 161-168, 1809. Also: Reil, Archiv., 12: 393-403, 1815.
2. On some physiological researches respecting the influence of the brain on the action of the heart, and on the generation

- of animal heat. *Phil. Trans.*, 101: 36-48, 1811. Also: London, W. Bulmer & Co., 1811. Roy. 8°, 15 pp. Also: Brugnatelli, *Giornale*, 5: 129-142, 1812. Also: Reil, *Archiv.*, 12: 137-155, 1815. (Same), London, Longman, 1851. 8°, vi, 146 pp., 1 pl. In A, C and D.
3. Experiments and observations on the different modes in which death is produced by certain vegetable poisons. *Phil. Trans.*, 101: 178-208, 1811. Also: London, W. Bulmer & Co., 1811. 4°, 31 pp. In A. Also: *Bull. de Phar.*, 55: 169-178, 1812. Also: Reil, *Archiv.*, 12: 156-198, 1815.
 4. Further experiments and observations on the action of poisons on the animal system. *Phil. Trans.*, 205-227, 1812. Also: *Annal. de Chimie*, 92: 5-31, 1815. Also: Reil, *Archiv.*, 12: 223-254, 1815.
 5. Further experiments and observations on the influence of the brain on the generation of animal heat. *Phil. Trans.*, 378-393, 1812. Also: *Jour. de Phys.*, 76: 386-387, 1813. Also: Nicholson, *Jour.*, 34: 199-211, 1813. Also: Gilbert, *Annalen*, 46: 80-93, 1814. Also: Reil, *Archiv.*, 12: 199-222, 1815.
 6. On abscess in the brain. *Trans. Soc. for Improvement of Med. & Chir. Knowledge*, 1812.
 7. Pathological researches respecting the diseases of joints. *Med.-Chir. Trans.*, 4: 207-277, 1813.
 8. The Croonian lecture for 1813. On the influence of the nervous system on the action of the muscles in general and of the heart in particular. (Printed from the Archives of the Royal Society, Works of Sir. B. C. Brodie, ed. by C. Hawkins.) Lond., 2: 97, 1865.
 9. Experiments and observations on the influence of the nerves of the eighth pair on the secretions of the stomach. *Phil. Trans.*, 102-106, 1814.
 10. Further observations on the diseases which affect the synovial membranes of joints. *Med.-Chir. Trans.*, 5: 239-254, 1814.
 11. Case of ununited fracture of the femur successfully treated by the introduction of a seton. *Ibid.*, 387.

12. Further observations on the ulceration of the cartilages of joints. *Ibid.*, 6: 318, 1815.
13. Observations on the treatment of varicose veins of the leg. *Ibid.*, 7: 195, 1816.
14. Pathological and surgical observations on diseases of the joints. London, Longman, 1818. 8°, vii, 329 pp. In A. C. D and E.
 (Same) *Traité des maladies des articulations*. Trans. by Léon Marchand. Paris, Plancher, 1819. 8°, xvi, 248 pp. In A.
 (Same) Philadelphia, Warner, 1821. 8°, vii, 329 pp., 6 pl. In A, C, D and E.
 (Same) *Pathologische und Chirurgische Beobachtungen über die Krankheiten der Gelenke*. Trans. with notes and additions by G. P. Holscher. Hannover, Hahn, 1821. 8°, xvi, 400 pp. 11., 6 pl., (2 col'd.). In A and C.
 (Same) 2. ed., London, Longman, 1822. 8°, vii, 376 pp., 8 pl. In A and C.
 (Same) *Over de ziekten der gewrichten*. Trans. with notes and additions by Hend. Sim. Hijmans. Haarlem, bij de Wed. A. Loosjes, Pz., 1823. 8°, viii, 317 pp. In A.
 (Same) 3. ed., London, 1834. In E.
 (Same) 3. ed., Washington, Green, 1834. 8°, vii, 131 pp. In A, C, D and E.
 (Same) 4. ed., London, Longman, 1836. 8°, xi, 354 pp. In C and D.
 (Same) From 4. London ed., Boston, Marvin, 1842. 8°, viii, 343 pp. In A, B, C, D and E.
 (Same) Philadelphia, Lea and Blanchard 1843. 8°, 216 pp. In A, C, D and E.
 (Same) From 4. London ed., Philadelphia, Lea and Blanchard; 1847. In D.
 (Same) 5. ed., 1850. 8°, vii, 349 pp. In A, B, C, D and E.
 (Same) *Abhandlung über die Krankheiten der Gelenke*. (Translated from the enlarged 5. English ed. and augmented by an appendix including the experiences of German and French surgeons, completed by G. A. Soer.) Coblenz, Hölscher, 1853. 8°, vii, 400 pp. In A.

15. Introductory lecture—Royal College of Surgeons. London, Burgess and Hill, 1820. 8°, 2 p. 1., 50 pp. In A and C.
16. Observations on the effects produced by the bile in the process of digestion. *Quart. Jour. Sc.*, 14: 341-344, 1823. Also: *Froriep, Notizen*, 4: Col. 177-180, 1823. Also: *Magendie, Jour. de Phys.* 3: 93-94, 1823.
17. Diseases of the urethra, bladder and prostate gland. *London Med. Gaz.*, 1: 4-8; 49-53, 1827; (stricture) 105-110; 169-173; 233-237; (irritable bladder) 297-301; (prostate) 393-397; 457-460; (treatment of chronic enlargement of prostate gland) 521-525.
18. Pathological and surgical observations relating to injuries of the brain. *Med.-Chir. Trans.*, 14: 325, 1828.
19. Experiments and observations intended to explain the mode in which death is produced by lightning. *Lond. Med. Gaz.*, 1: 79-81, 1828.
20. Needles extracted from various parts of the body. *Ibid.*, 148-149.
21. Cysts containing watery fluid, apparently connected with the liver. *Ibid.*, 334-335.
22. On trephining the tibia. *Ibid.*, 2: 70-74.
23. Injuries of the brain. *Ibid.*, 134-139; 199-205; 230-235; 297-302; 357-363.
24. Peculiar affection of the wrist, occurring in hysterical patients. *Ibid.*, 755-756.
25. Clinical lecture on effusion of urine. *Ibid.*, 3: 25-27, 1829.
26. Case of aneurysm by anastomosis of the forehead treated by the application of ligatures. *Med.-Chir. Trans.*, 15: 177, 1829.
27. On conduct and duties of medical practitioner. *Lond. Med. Gaz.* 5: 39-45, 1829.
28. Observations on certain local nervous affections. *Ibid.*, 553-562, 1830.
29. Use of iodine in morbid growths. *Ibid.*, 750-751.
30. Observations on calculus diseases. *Ibid.*, 8: 1-8, 1831. (renal calculi) 65-71; (calculi of bladder) 129-137; 225-229; 353-358; (operation of lithotomy) 609-616; 833-842.

31. An account of some cases of chronic abscess of the tibia. Med.-Chir. Trans. 17: 239-249, 1832.
32. Brief account of ligature of subclavian artery. Lond. Med. Gaz., 9: 395-396, 1832.
33. Account of a clinical lecture on hydrocele and hematocele. Ibid., 926-929.
34. Case of amputation at the shoulder joint. Ibid., 11: 300-303, 1833.
35. Lectures on diseases of the urinary organs. London, Longman, 1832. 8°, viii, 306 pp. In A and C.
 (Same) Vorlesungen über die Krankheiten der Harnmerkmale. Weinar, 1833. 8°, vi, 150 pp., pl. In A and C.
 (Same) 2. ed., London, Longman, 1853. 8°, viii, 329 pp. In C and D.
 (Same) Vorlesungen über die vorzüglichsten Krankheiten der Harnaussführungsorgane. Leipzig, 1836. 8°, In A.
 (Same) 3. ed. London, Longman, 1842. 8°, vii, 379 pp. In A and D.
 (Same) From 3. London ed., Philadelphia, Lea and Blanchard, 1843. 8°, 214 pp. In A, B, C, D and E.
 (Same) 2. Amer. from last London ed., Philadelphia, Lea and Blanchard, 1847. In D and E.
 (Same) 4. ed., London, Longman, 1849. 8°, vii, 392 pp. In A, C and E.
 (Same) Translated into French by Patron, Montpellier.
36. Ununited fractures. Lond. Med. Gaz., 13: 53-59, 1833.
37. Diseases of the testicle. Ibid., (hydrocele) 88-94; 136-140; (inflammation) 218-223; (tuberculosis) 377-382; (fungus hematodes) 407-410; 618-622.
38. Clinical observations on ununited fractures. Ibid., 14: 616-618, 1834.
39. Clinical observations on fatty tumors. Ibid., 679-681.
40. On encysted tumors. Ibid. 15: 25-27, 1835.
41. On diseases of the maxillary antrum. Ibid., 346-351.
42. On hemorrhoids. Ibid., 742-747; (prolapsus) 842-847.
43. On diseases of rectum, cont'd., (preternatural contraction of sphincter ani). Ibid., 16: 26-31; 236-239, 1835.

44. Diseases of rectum, cont'd., (abscesses, fistula). Ibid., 17: 25-29; 485-490; 18: 182-187, 1835.
45. Outline of paper on pathological and surgical observations to injuries of spinal cord. Ibid., 379-381.
46. On tic douloureux or facial neuralgia. Ibid., 534-539.
47. A case of compound fracture of tibia followed by traumatic delirium. Ibid., 613-616.
48. On corns and bunions. Ibid., 775-780.
49. On local hysterical affections. Ibid., 19: 197-201; 246-250; 279-286, 1837.
50. Extracts from Hunterian Oration. Ibid., 969-972.
51. The Hunterian oration, 1837. London, Longman, 1837. 8°, 38 pp. In A.
52. Lectures illustrative of certain local nervous affections. London, Longman, 1837. 8°, iv, 88 pp. In A B, C, D and E.
(Same) in Dunglison's Amer. Med. Library, Philadelphia, 1838. pp. 33-74
(Same) Vorlesungen über örtliche Nervenleiden. Aus dem Englischen von Dr. Kürschner. Marburg, Garthe, 1838. 8°, iv, 65 pp. In A.
53. Pathological and surgical observations relating to injuries of the spinal cord. Med.-Chir. Trans., 20: 118, 1837. Also: in Dunglison's Amer. Med. Library, Philadelphia 1838, pp. 451-474
54. An introductory discourse on the studies required for the medical profession. London, Brettell, 1838. 8°, 32 pp. In A.
55. On diseases of the kidney. Lond. Med. Gaz., 21: 106-109, 1838.
56. On varicose veins and ulcers of the legs. Ibid., 184-189; 264-268.
57. On sero-cystic tumors of the breast. Ibid., 25: 808-814, 1840.
58. Lectures on mortification. Ibid., 27: 471-477; 536-540; 601-608; 745-750, 1841. (hospital gangrene) 633-636; (senile gangrene) 714-719.

59. An account of two cases of imperforate hymen. (Review).
Ibid., 810-811.
60. Eulogium on Sir Astley Cooper, delivered at a meeting of the
Royal Medical and Chirurgical Society. Lond. Med.
Gaz., 27: 884-886, 1841.
61. Lectures illustrative of some important circumstances con-
nected with operative surgery. Ibid., 31: 388-393; 641-
648, 1842.
62. On quacks and quackery. 1842.
63. Clinical lectures on surgery. Med. News and Library, vol.
1-3, 1843-1845.
64. An introductory discourse on the duties and conduct of
medical students and practitioners. Lond. Med. Gaz.,
33: 97-105, 1843. Also: London, Mitchell, 1843. 8°,
34 pp. In A and C.
(Same) Over de pligten en den levenswandel van studenten
in de medicijnen en jeugdige geneesheeren. Vertaald door
Rudolf Ruben. Amersfoort, W. J. van Bommel van
Vloten, 1844. 8°, 33 pp. In A.
65. Brief report of a case in which a foreign body was lodged in
the right bronchus. Lond. Med. Gaz., 32: 540-541; 33:
215-216, 1843.
66. Abscess and fistula connected with the rectum. Ibid., 33:
515-521; 554-558; 584-589, 1844.
67. Cases in which it is expedient to perform the operation for
the removal of scirrhus tumor of the female breast. Ibid.,
628-833; continued, with administration of mercury in
cases of syphilis. Ibid., 664-671.
68. Some diseases of the breast. Med. Times, 10: 163, 1844.
69. Lecture on abscess of the tibia. Lond. Med. Gaz., 36:
1399-1403, 1845.
70. Lectures on diseases of the knee joint. Ibid., 37: 221-225;
397-402; 489-493; 623-627, 1846.
71. Discourse on the mode of investigating the sciences belonging
to the medical profession. Ibid., 38: 603-613.
72. Lectures on distortion of the spine not connected with
caries. Ibid., 999-1003; 39: 1-6; 89-93.

73. Clinical lectures on surgery, delivered at St. George's Hospital. Philadelphia, Lea and Blanchard, 1846. 8°, viii, 352 pp. In A, B, C, D and E.
74. Lectures illustrative of various subjects in pathology and surgery. London, Longman, 1846. 8°, vii, 411 pp. In A, C and D.
75. Chemical relations of wax and fat. Lond. Med. Gaz., 53: 474-475, 1849.
76. Address at the Ethnological Society of London, delivered at the annual meeting on the 26th of May, 1854. London, Watts, 1854. 8°, 25 pp. In A.
77. Psychological inquiries: mind and matter: in a series of essays, intended to illustrate the mutual relations of the physical organization and the mental faculties. 2. ed., London, Longman, 1855. 12°, xii, 275 pp. In A, C and D. (1. ed., 1854, anonymous.)
 (Same) With additional notes by an American editor. New York, Putnam, 1857. 12°, viii, 279 pp. In A, C, D and E.
 (Same) New York, Wood, 1858. 8°, viii, 279 pp. In A and D.
 (Same) The second part being a series of essays intended to illustrate some points in the physical and moral history of man. London, 1862. 12°, xi, 247 pp. In C and E.
 (Same) New York, Wood, 1873. In D.
78. Notes on lithotrity, with an account of the results of the operation in the author's practice. Med.-Chir. Trans., 38: 169, 1855.
79. Case of myeloid (?) tumour of bone. (Notice) Ibid., 39: 122, 1856.
80. The healing art the right hand of the church: or practical medicine an essential element in the Christian system. By Therapeuts. Edinburgh, Sutherland & Knox, 1859. 8°, 3 p. 1., 280 pp. In A.
81. President's address delivered at the anniversary meeting of the Royal Society, Nov. 30, 1859. London, Taylor & Francis, 1859. 8°, 20 pp. In A.
82. The use and abuse of tobacco. (London, 1860) 8°, 16 pp. In A.

83. Notice on a case of calculus, mixed with teeth, hair, etc. Med.-Chir. Trans., 43: 109, 1860.
84. Homeopathy: a letter to J. S. S., Esq. London, Parker, 1861. 8°, 8 pp. In A.
85. Letter on Dr. Bullar's case of pulsating bronchocele. Med.-Chir. Trans., 44: 38, 1861.
86. Letter on Dr. Water's paper on asphyxia and the use of the hot bath. Ibid., 149.
87. The works of Sir Benjamin Collins Brodie with an autobiography. Collected and arranged by Charles Hawkins. London, Longman, 1865. 8°, 3 vols. In A. C, D and E.

BIOGRAPHIES

- Biography by Pettigrew. Med. Port. Gallery, II, vol. 5, 16 pp., London, 1840.
- Biography. Lancet, 1: 538-544, 1850.
- The medical case of Sir Benjamin Brodie; the operation on his eyes. Boston Med. & Surg. Jour., 62: 467, 1861.
- Biography. Lancet, 2: 452-457, 1862.
- Biography. Med. Times & Gaz., 2: 452; 474; 504, 1862.
- Biography. Wien. med. Woch., 12: 732; 748, 1862.
- Biography by Giraldes. Bull. Soc. de Chir. de Paris, 3: 606-631, 1863.
- Biography by H. W. Acland. London, 1864. 12°, 31 pp.
- Autobiography. (With The Works of Sir Benjamin Collins Brodie, collected and arranged by Charles Hawkins.) London, Longman, 1865. 8°, 3 vols.
- Biography by J. Althaus. Deutsche Klinik, 18: 241; 253, 1866.
- Biography by R. E. Thompson. Dict. Nat. Biog., 6: 378-380, 1886.
- Masters of medicine: Benjamin Brodie. By T. Holmes. London, Unwin, 1898. 8°, 256 pp.
- Biography. Practitioner, 61: 381-387, 1898.
- Biography. Boston Med. & Surg. Jour., 140: 369-373, 1899.
- Biography. Brit. Jour. Surg., 6: 157-159, 1918.
- Brodie's tumor and Brodie's abscess: eponyms. By Sir D'A. Power. Brit. Jour. Surg., 9: 334-337, 1922.
- Sketch. Lancet, 2: 709, 1923.

73. Clinical lectures on surgery, delivered at St. George's Hospital. Philadelphia, Lea and Blanchard, 1846. 8°, viii, 352 pp. In A, B, C, D and E.
74. Lectures illustrative of various subjects in pathology and surgery. London, Longman, 1846. 8°, vii, 411 pp. In A, C and D.
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 (Same) New York, Wood, 1873. In D.
78. Notes on lithotrity, with an account of the results of the operation in the author's practice. Med.-Chir. Trans., 38: 169, 1855.
79. Case of myeloid (?) tumour of bone. (Notice) Ibid., 39: 122, 1856.
80. The healing art the right hand of the church: or practical medicine an essential element in the Christian system. By Therapeuts. Edinburgh, Sutherland & Knox, 1859. 8°, 3 p. 1., 280 pp. In A.
81. President's address delivered at the anniversary meeting of the Royal Society, Nov. 30, 1859. London, Taylor & Francis, 1859. 8°, 20 pp. In A.
82. The use and abuse of tobacco. (London, 1860) 8°, 16 pp. In A.

83. Notice on a case of calculus, mixed with teeth, hair, etc. Med.-Chir. Trans., 43: 109, 1860.
84. Homeopathy: a letter to J. S. S., Esq. London, Parker, 1861. 8°, 8 pp. In A.
85. Letter on Dr. Bullar's case of pulsating bronchocele. Med.-Chir. Trans., 44: 38, 1861.
86. Letter on Dr. Water's paper on asphyxia and the use of the hot bath. Ibid., 149.
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- Biography by Pettigrew. Med. Port. Gallery, II, vol. 5, 16 pp., London, 1840.
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- The medical case of Sir Benjamin Brodie; the operation on his eyes. Boston Med. & Surg. Jour., 62: 467, 1861.
- Biography. Lancet, 2: 452-457, 1862.
- Biography. Med. Times & Gaz., 2: 452; 474; 504, 1862.
- Biography. Wien. med. Woch., 12: 732; 748, 1862.
- Biography by Giralde. Bull. Soc. de Chir. de Paris, 3: 606-631, 1863.
- Biography by H. W. Acland. London, 1864. 12°, 31 pp.
- Autobiography. (With The Works of Sir Benjamin Collins Brodie, collected and arranged by Charles Hawkins.) London, Longman, 1865. 8°, 3 vols.
- Biography by J. Althaus. Deutsche Klinik, 18: 241; 253, 1866.
- Biography by R. E. Thompson. Dict. Nat. Biog., 6: 378-380, 1886.
- Masters of medicine: Benjamin Brodie. By T. Holmes. London, Unwin, 1898. 8 , 256 pp.
- Biography. Practitioner, 61: 381-387, 1898.
- Biography. Boston Med. & Surg. Jour., 140: 369-373, 1899.
- Biography. Brit. Jour. Surg., 6: 157-159, 1918.
- Brodie's tumor and Brodie's abscess: eponyms. By Sir D'A. Power. Brit. Jour. Surg., 9: 334-337, 1922.
- Sketch. Lancet, 2: 709, 1923.

Biographical sketch. *New England Jour. Med.*, 203: 749-750, 1930.

Biography by H. E. Mansell. *Lancet*, 2: 408-419, 1935.

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INTRODUCTION

Benjamin Collins Brodie obtained for his day an excellent medical education. In London he studied anatomy under Abernethy at St. Bartholomew's Hospital and also worked under James Wilson at the Great Windmill Street School of Medicine. At the age of twenty he was a pupil of Sir Everard Home at St. George's Hospital and two years later became House Surgeon there. Dr. Home then employed Brodie as his assistant and at the age of twenty-five we find Brodie actively at work at St. George's Hospital as Assistant Surgeon.

The very next year, in 1809, at the age of twenty-six we find Brodie publishing his first paper, *Account of the dissection of a human fetus in which the circulation of the blood was carried on without a heart.*

In 1811 he published two papers, the first on the influence of the brain on the action of the heart and the second on the effects of certain vegetable poisons. In the following year he wrote on the influence of the nervous system on the production of animal heat and in 1813 he first described a disease of joints which is now called by his name.

Benjamin Brodie rapidly rose in the medical world and at the age of thirty-six became Professor of Comparative Anatomy and Physiology at the Royal College of Surgeons. At the age of thirty-nine he became full surgeon at St. George's Hospital. In 1828 at the age of forty-five, he was appointed surgeon to King George IV and four years later Serjeant-Surgeon to William IV.

In this same year, 1832, he published a paper, *An account of some cases of chronic abscess of tibia.* For a long time he had been particularly interested in diseases of bones and joints, fourteen years previously having written a book on *Pathological and surgical observations on diseases of the joints* which went through five editions and was translated into French, German and Dutch.

The paper of 1832 is reproduced on the following pages as it was first printed; it is in reality a series of case reports which Brodie had collected from his experience as surgeon to St. George's Hospital. Case I concerns a young man who died following an amputation of the leg for a chronic osteomyelitis of twelve years duration. Without the aid of x-rays, Brodie was unable to foresee an abscess within the tibia. After amputation and the fatal

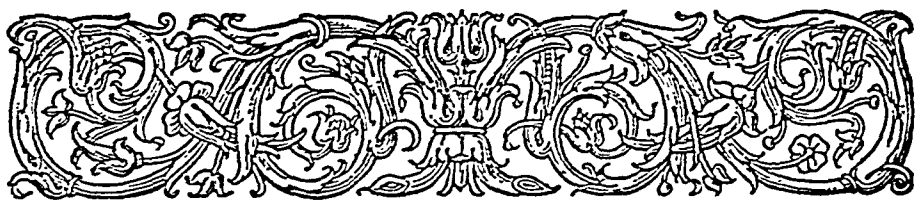
outcome he determined at his next opportunity to trephine the bone and probably save both life and limb. A year and a half later, however, Brodie frankly admits that a second case was treated by a simple incision through the periosteum. Almost two years later it became necessary to again operate on this patient and this time Brodie trephined the bone abscess and was rewarded with a cure. The third patient benefited by the experiences with the other two, was operated on by trephining the bone and recovered.

In 1834 at the age of fifty-one, Brodie was raised to the rank of Baronet.

In 1835 he delivered a series of lectures on diseases of the rectum at St. George's Hospital. Lecture number three treated of preternatural contraction of the sphincter ani. This paper is reproduced on the following pages in its complete and original form. The work shows a great interest in the subject of rectal disease and a wide knowledge of rectal pathology. Brodie described a pathologic finding which has become known as Brodie's pile and also an operation for fissure or ulcer of anus which is still known by his name. The paper is important because it reveals the teaching of a hundred years ago of this famous surgeon and describes a condition and an operation which are still known and used today.

The last paper of Sir William Collins Brodie which is reproduced here is a *Lecture on sero-cystic tumors of the breast* delivered at St. George's Hospital in 1840. The subject was chosen by Brodie because he had attended many patients with the condition and because he felt his experience would be helpful to the younger practitioners. He promptly states in the second paragraph that he is not describing a new disease, Sir Astley Cooper and M. Velpeau both having written on the subject. But Brodie's description of the clinical manifestations and gross pathology are so clear and exact that the condition to this day is called Brodie's tumor. The paper is an important one in the progress of knowledge of diseases of the breast.

Late in life Sir William Collins Brodie was elected president of the Royal College of Surgeons, of the General Medical Council and of the Royal Society. He was acknowledged leader of the medical profession of London and it is fitting that his name is remembered by numerous medical eponyms.



Brodie's Abscess

An Account of Some Cases of Chronic
Abscess of the Tibia

BY

B. C. BRODIE, F. R. S.

Surgeon to St. George's Hospital

Read March 27th, 1832. Published in *Medico-Chirurgical Transactions*, London, 17:
239-249, 1832

IAM not aware that any cases exactly similar to those which I am about to relate have been recorded by authors: and as they appear to me to throw some light on the history and treatment of a rare but very serious disease, I am led to believe that they are not unworthy of being communicated to the Medical and Chirurgical Society.

CASE I

Mr. P., about twenty-four years of age, consulted me in October, 1824, under the following circumstances.

There was a considerable enlargement of the lower extremity of the right tibia, extending to the distance of two or three inches from the ankle-joint. The integuments at this part were tense, and they adhered closely to the surface of the bone.

(p. 240) The patient complained of a constant pain referred to the enlarged bone, and neighbouring parts. The pain was always sufficiently distressing; but he was also liable to more severe paroxysms in which his sufferings were described as most excruciating. These paroxysms recurred at irregular intervals,

confining him to his room for many successive days, and being attended with a considerable degree of constitutional disturbance. Mr. P. described the disease as having existed more than twelve years, and as having rendered his life miserable during the whole of that period.

In the course of this time he had been under the care of various surgeons, and various modes of treatment had been resorted to without any permanent advantage. The remedies which I prescribed for him were equally inefficacious. Finding himself without any prospect of being relieved by other means, he made up his mind to lose the limb by amputation; and Mr. Travers having seen him with me in consultation, and having concurred in the opinion, that this was the best course which could be pursued, the operating was performed accordingly.*

(p. 241) On examining the amputated limb, it was found that a quantity of new bone had been deposited on the surface of the lower extremity of the tibia. This deposition of new bone was manifestly the result of inflammation of the periosteum at some former period. It was not less than one-third of an inch in thickness, and when the tibia was divided longitudinally with a saw, the line at which the new and old bone were united with each other, was distinctly to be seen.

The whole of the lower extremity of the tibia was harder and

*It is right that I should state briefly the termination of the case; especially as the circumstances attending it were probably connected with a peculiar condition of the nervous system occasioned by the long continuance of the local disease. Unfortunately I preserved no notes of this part of the case at the time, but I have no doubt that my recollection is accurate as to the following particulars. The patient bore the operation with the utmost fortitude, but immediately afterwards he was observed to become exceedingly irritable, restless, and too much disposed to talk. Unfortunately in the evening there was hæmorrhage from the stump, which ceased, however, on the removal of the dressings and coagulum. During the night he had no sleep; and on the following day he was restless, and incessantly talking, with a rapid pulse. These symptoms became aggravated. There was no disposition to sleep, and the pulse became so rapid that it could be scarcely reckoned. Until the third or fourth day the tongue remained clean and moist. After this period it became dry, and somewhat brown, and there was constant delirium. The pupils were widely dilated, and the sensibility of the retina was totally destroyed, the glare of a candle not being perceptible even when held close to the eye. Death took place on the fifth day after the operation. No morbid appearances were observed in the *post-mortem* examination.

more compact than under ordinary circumstances, in consequence, as it appeared, of some deposit of bone in the cancellous structure, and in its centre, about one-third of an inch above the ankle, (p. 242) there was a cavity of the size of an ordinary walnut, filled with a dark-coloured pus. The bone immediately surrounding this cavity, was distinguished from that in the neighbourhood by its being of a whiter colour, and of a still harder texture, and the inner surface of the cavity presented an appearance of high vascularity. The ankle-joint was free from disease.

It is evident that if the exact nature of the disease had been understood, and the bone had been perforated with a trephine, so as to allow the pus collected in its interior to escape, a cure would probably have been effected, without the loss of the limb, and with little or no danger to the patient's life. Such, at least, was the opinion which the circumstances of the case led me to form at the time; and I bore them in my mind, in the expectation that at some future period I might have the opportunity of acting on the knowledge which they afforded me for the benefit of another patient.

CASE II

Mr. B., at that time twenty-three years of age, consulted me in the beginning of February, 1826.

There was a considerable enlargement of the right tibia, beginning immediately below the knee, and extending downwards so as to occupy about one-third of the length of the bone.

(p. 243) Mr. B. complained of excessive pain, which disturbed his rest at night, and some parts of the swelling were tender to the touch. The knee itself was not swollen, and its motions were perfect.

He said that the disease had begun more than ten years ago, with a slight enlargement and pain in the upper extremity of the tibia; and that these symptoms had gradually increased up to the time of my being consulted. Various remedies had been employed, from which, however, he had derived little or no advantage.

Having inquired into the circumstances of the case, I was led

to regard it as one of chronic periostitis; and I adopted the following method of treatment. An incision was made longitudinally on the anterior and inner part of the tibia, extending from the knee four inches downwards, and penetrating through the periosteum into the substance of the bone. The periosteum was found considerably thickened, and the new bone, which had been deposited beneath, was soft and vascular. The immediate effect of the operation was to relieve the pain which the patient suffered, so that he slept well on the next and every succeeding night. After this I prescribed for him a strong decoction of sarsaparilla. The wound gradually healed, and it was for some time supposed that a perfect cure had been accomplished.

(p. 244) The enlargement of the upper extremity of the tibia, however, never entirely subsided; and in August 1827 pain was again experienced in it. At first the pain was trifling, but it gradually increased, and when I was again consulted, in January 1828, Mr. B. was unable to walk about, and quite unfit for his usual occupations. At this period the pain was constant, but more severe at one time than at another, often preventing sleep during several successive nights. The enlargement of the tibia was as great as when I was first consulted; and the skin covering it was tense and adhering more closely than is natural to the surface of the bone.

Some remedies which I prescribed were productive of no benefit. The patient's sufferings were excruciating, and it was necessary that he should, if possible, obtain immediate relief. The resemblance between the symptoms of this case and those of the case already described, were too obvious to be overlooked. It appeared highly probable that they depended on the same cause; and I therefore proposed that the bone should be perforated with a trephine, in the expectation that an abscess would be discovered in its interior. To this the patient readily assented, and accordingly the operation was performed in the beginning of March 1828.

My attention was directed to a spot about two inches below the knee, to which the pain was particularly referred. This part of the tibia was exposed by a crucial incision of the integuments.

more compact than under ordinary circumstances, in consequence, as it appeared, of some deposit of bone in the cancellous structure, and in its centre, about one-third of an inch above the ankle, (p. 242) there was a cavity of the size of an ordinary walnut, filled with a dark-coloured pus. The bone immediately surrounding this cavity, was distinguished from that in the neighbourhood by its being of a whiter colour, and of a still harder texture, and the inner surface of the cavity presented an appearance of high vascularity. The ankle-joint was free from disease.

It is evident that if the exact nature of the disease had been understood, and the bone had been perforated with a trephine, so as to allow the pus collected in its interior to escape, a cure would probably have been effected, without the loss of the limb, and with little or no danger to the patient's life. Such, at least, was the opinion which the circumstances of the case led me to form at the time; and I bore them in my mind, in the expectation that at some future period I might have the opportunity of acting on the knowledge which they afforded me for the benefit of another patient.

CASE II

Mr. B., at that time twenty-three years of age, consulted me in the beginning of February, 1826.

There was a considerable enlargement of the right tibia, beginning immediately below the knee, and extending downwards so as to occupy about one-third of the length of the bone.

(p. 243) Mr. B. complained of excessive pain, which disturbed his rest at night, and some parts of the swelling were tender to the touch. The knee itself was not swollen, and its motions were perfect.

He said that the disease had begun more than ten years ago, with a slight enlargement and pain in the upper extremity of the tibia; and that these symptoms had gradually increased up to the time of my being consulted. Various remedies had been employed, from which, however, he had derived little or no advantage.

Having inquired into the circumstances of the case, I was led

to regard it as one of chronic periostitis; and I adopted the following method of treatment. An incision was made longitudinally on the anterior and inner part of the tibia, extending from the knee four inches downwards, and penetrating through the periosteum into the substance of the bone. The periosteum was found considerably thickened, and the new bone, which had been deposited beneath, was soft and vascular. The immediate effect of the operation was to relieve the pain which the patient suffered, so that he slept well on the next and every succeeding night. After this I prescribed for him a strong decoction of sarsaparilla. The wound gradually healed, and it was for some time supposed that a perfect cure had been accomplished.

(p. 244) The enlargement of the upper extremity of the tibia, however, never entirely subsided; and in August 1827 pain was again experienced in it. At first the pain was trifling, but it gradually increased, and when I was again consulted, in January 1828, Mr. B. was unable to walk about, and quite unfit for his usual occupations. At this period the pain was constant, but more severe at one time than at another, often preventing sleep during several successive nights. The enlargement of the tibia was as great as when I was first consulted; and the skin covering it was tense and adhering more closely than is natural to the surface of the bone.

Some remedies which I prescribed were productive of no benefit. The patient's sufferings were excruciating, and it was necessary that he should, if possible, obtain immediate relief. The resemblance between the symptoms of this case and those of the case already described, were too obvious to be overlooked. It appeared highly probable that they depended on the same cause; and I therefore proposed that the bone should be perforated with a trephine, in the expectation that an abscess would be discovered in its interior. To this the patient readily assented, and accordingly the operation was performed in the beginning of March 1828.

My attention was directed to a spot about two inches below the knee, to which the pain was particularly referred. This part of the tibia was exposed by a crucial incision of the integuments.

The periosteum now was not in the same state as at the time of the former operation. It was scarcely thicker than natural, and the bone beneath was hard and compact. A trephine of a middle size was applied, and a circle of bone was removed extending in to the cancellous structure, but no abscess was discovered. I then, by means of a chisel, removed several other small portions of bone at the bottom of the cavity made by the trephine. As I was proceeding in this part of the operation the patient suddenly experienced a sensation, which he afterwards described as being similar to that which is produced by touching the cavity of a carious tooth, but much more severe, and immediately some dark coloured pus was seen to issue slowly from the part to which the chisel had been last applied. This was absorbed by a sponge, so that the quantity of pus which escaped was not accurately measured, but it appeared to amount in all to about two drams. From this instant the peculiar pain belonging to the disease entirely ceased, and it has never returned. The patient experienced a good deal of pain, the consequence of the operation, for the first twenty-four hours, after which there was little or no suffering. The wound was dressed lightly to the bottom with lint. Nearly six months elapsed before it was completely cicatrized: but in about three months from the day of the operation, Mr. B. was enabled to walk about and attend to his usual occupations. He has continued well to the present time (January 7, 1832); and the tibia is now reduced in (p. 246) size so as to be scarcely larger than that of the other leg. No exfoliation of bone has ever taken place.

CASE III

In the beginning of January 1830, Mr. S., thirty-four years of age, consulted me on account of the following symptoms.

The lower extremity of the left tibia was considerably enlarged; the skin covering it was tense, and adhered closely to the parts below. The patient complained of a constant aching pain, which he referred to the enlarged bone. Once in two or three weeks there was an attack of pain more severe than usual, during which his sufferings were excruciating, lasting several hours, and some-

times one or two days, and rendering him altogether incapable of following his usual occupations. The pain was described as shooting and throbbing, worse during the night, and attended with such exquisite tenderness of the parts in the neighbourhood of the ankle that the slightest touch was intolerable.

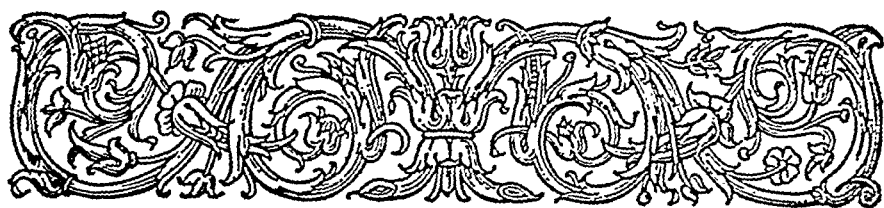
Mr. S. said, that to the best of his recollection, the disease had begun eighteen years ago, in the following manner. On going to bed one evening he suddenly experienced a most acute pain in the inner ankle. On the following morning he was unable to put his foot to the ground, on account of the agony which every attempt to do so occasioned. Leeches (p. 247) were applied several times, and afterwards blisters, but the pain increased notwithstanding. After some weeks an abscess presented itself and broke. This was followed by some mitigation of the symptoms. Soon afterwards another abscess formed and broke in the neighbourhood of the first. The two abscesses remained open for a considerable time, and then healed rapidly. Mr. S. now began to regain the use of the limb, and by degrees was able to walk as usual.

During the following summer he had a recurrence of pain in the inner ankle, without any further formation of abscess. For eight or ten years afterwards there were occasional attacks of pain, lasting one or two days at a time; the intervals between them being of various duration, and in one instance, not less than nine months. After this the attacks recurred more frequently, and during the whole of the last two years the symptoms were nearly as severe as at the time of my being consulted.

On examining the limb I was struck with the resemblance which it bore to that of the limb in each of the two preceding cases. There was also a remarkable resemblance in the symptoms as described by the patient, and I could not but suspect that they depended on a similar cause. I requested that Mr. Travers, who had attended one of the former cases with me, should be consulted; and he agreed with me in the opinion that probably an abscess existed in (p. 248) the centre of the tibia, and that it would be advisable to perforate the bone with a trephine, with the view of enabling the contents of the abscess to escape.

Accordingly I performed the operation, with the assistance of Mr. Travers, on the 31st of January. A crucial incision was made through the skin, the angles of which were raised so as to expose a part of the bone above the inner ankle, to which the pain was especially referred. A small trephine was then applied, and a circular portion of bone was removed extending into the cancellous structure. Other portions of bone were removed with a narrow chisel. At last about a dram of pus suddenly escaped and rose into the opening made by the trephine and chisel. On further examination a cavity was discovered from which the pus had flowed, capable of admitting the extremity of the finger. The inner surface of this cavity was exquisitely tender; the patient experiencing the most excruciating pain on the gentlest introduction of the probe into it.

He passed a tolerable night, and suffered but little on the following day. He continued to go on favourably until the 5th of February, when a violent inflammation attacked the limb immediately above the inner ankle. In spite of the application of leeches, an abscess formed, which in the course of six or seven days, presented itself immediately below the part at which the trephine had been applied. An opening was made with a lancet, and a considerable quantity (p. 249) of pus escaped, which had apparently formed between the periosteum and bone, the latter being felt exposed at the bottom of the abscess. During the following month the inflammation excited by the operation continued, and several abscesses presented themselves in the neighbourhood of the first. These however all healed favourably without any exfoliation of bone taking place. The cavity made by the trephine became filled up by granulation, and the wound gradually cicatrized. From the time of the operation, the peculiar pain from which the patient had previously suffered, was entirely relieved: and it was not long before he was quite restored to health, and able to walk and pursue his occupations without interruption. I have seen him lately, nearly two years from the time of the operation having been performed, and he continues perfectly well.



Brodie's Abscess

Lecture on Abscess of the Tibia

BY

SIR B. C. BRODIE, BART.

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I SHALL not make any introductory observations to the course of lectures which I am about to deliver, further than these—that on this, as on former occasions, I do not pretend to give any systematic course, but to select various subjects in which I suppose you will feel interested, and such especially as you will find to be of importance in surgical practice. If I do not enter into the consideration of abstract questions in physiology and pathology, it is not because I regard these subjects as unimportant, but because I think it still more important that in the few lectures which I shall deliver I should contribute as much as I can towards making you useful to the public and to yourselves as good practical surgeons.

The subject that I shall take for the present lecture, is one of considerable interest, namely, the formation of abscess in the interior of the tibia.

I need not tell you that bones are organized like soft parts; that they have the same apparatus of arteries, veins, nerves, and cellular tissue, and that they have superadded to these the unorganized phosphate of lime. Having the same tissues as the soft parts, they are liable to very much the same diseases, but then the characters of these diseases, their symptoms, progress, and treat-

ment, are much modified by the presence of the unyielding earthy material which I have mentioned. Inflammation may take place in bones, as it does elsewhere; it may go on to suppuration, and abscess may form in their interior, as it does in the interior of other organs. But there are these points of difference—an abscess formed in a bone cannot very readily come to the surface, so that it may remain pent up for an indefinite period: the soft parts will stretch, bones will not, and the consequence is, that an abscess situated in the latter is attended with much greater pain than that which occurs in the former. The patient's sufferings are consequently more severe, and they are protracted for a very much longer period.

I am not aware that I can explain to you better what I know on the subject, than by relating some of the cases on which my knowledge of it is founded.

In the year 1824, I was consulted by a young man, 24 years of age, under the following circumstances. There was a considerable enlargement of the lower end of the tibia, but the ankle-joint admitted of every motion, and was apparently sound. The skin was thin, tense, and closely adherent to the periosteum. There was constant pain in the part, generally of a moderate character, but every now and then it became excruciating, keeping the patient awake at night, and confining him to the house for many successive days. It made his life miserable, and his nervous system irritable: one effect of which was that it spoiled his temper, and thus produced another set of symptoms in addition to those which were the direct consequences of the local malady. The disease had been going on for 12 years. He had consulted a number of surgeons respecting it, and had never derived benefit from anything that was done. Instead of getting better, he every year became so much worse. I tried some remedies without any advantage, and at last recommended that he should lose the limb. Mr. Travers saw him with me, and agreed in this opinion. Amputation was performed, and the amputated tibia is now on the table. You will see how much the lower end of it is enlarged, and that the surface of it presents marks of great vascularity. The bone in the preparation is divided longi-

tudinally, and just above the articulating surface there is a cavity as large as a small chestnut. This cavity was filled with dark coloured pus. The inner surface of it is smooth. The bone immediately surrounding it is harder than natural. The examination of the limb explained all the symptoms: there was an abscess of the tibia, stretching the bone in which it was formed, or rather, if I may use the expression, trying to stretch it, and thus causing violent pain which the patient suffered. On observing these appearances, I could not help saying, that if we had known the real state of the disease, the limb might have been saved. A trephine would have made an opening in the tibia, and have let out the matter. It would have been merely applying the treatment here that we adopt in the case of abscess elsewhere. You open a painful abscess of the arm with a lancet; you cannot open an abscess of the bone with a lancet but you may do so with a trephine.

About two years after the occurrence of this case, I was consulted by another patient, 23 years of age, who had an enlargement of the upper end of the tibia, extending to some distance below the knee. He suffered a great deal of pain, the part was very tender, and there were all the symptoms of chronic periostitis. I made an incision over the part, dividing everything down to the (p. 1400) bone, and found the periosteum very much thickened. There was a new deposit of bone under the periosteum, softer than the bone of original formation. This operation as in other cases of chronic periostitis, relieved the tension and the pain, and the patient was supposed to be cured. However, about a year afterwards, in August 1827, there was a recurrence of the pain; the enlargement of the tibia, which had in some degree subsided, returned, and it continued to increase. In the enlarged tibia there was one spot a little below the knee, where there was exceeding tenderness on pressure. I need not describe the symptoms more particularly; it is sufficient to say, that they bore a very close resemblance to those in the last case: the only difference being that, as the disease had been of shorter duration, the pain was less severe, and that the tibia was affected in the upper instead of the lower extremity. I concluded that there

must be an abscess in the centre of the bone, and applied the trephine to the tender spot. I used the common trephine made for injuries of the head, which, having a projecting rim or shoulder, would penetrate only to a certain depth. However, it enabled me to remove a piece of bone of sufficient thickness to expose the cancellous structure. Then with a chisel I removed some more of the bone. Presently there was a flow of pus in such quantity as completely to fill the opening made by the trephine and the chisel. It seemed as if the bone had been, to a certain extent, kept on the stretch by the abscess, and that, as soon as an opening was made into it, it contracted and forced up the matter. The patient was well from that time; the wound healing very favourably, and he has never had any return of the disease.

Sometime after this I was consulted by a gentleman who had an enlargement of the lower end of the tibia. He suffered constant pain, but every two or three weeks there was an exacerbation of it, and it was then very excruciating, almost intolerable. These attacks sometimes lasted two or three days. This patient when he came under my care was 34 years of age; he traced the disease back for eighteen years, and stated that it began in the following manner; on going to bed one evening, he felt a sudden pain in or just above the ankle-joint; the next day there was a swelling in this situation, he was laid up with inflammation, and two abscesses burst in succession, but afterwards healed. He continued well for some considerable time, and then he was again seized with pain in the ankle. This pain was not constant, but occurred at intervals. Sometimes there were several months during which he was quite well. (These points are worthy of notice with respect to the diagnosis, as I shall show you presently.) After some years, however, the pain was never absent, and he got into the state in which he was when he sought my advice. On examining the ankle I found the tibia considerably enlarged. The motion of the joint was perfect, but there was one tender spot on the inside of the bone that seemed to indicate the seat of an abscess. I applied a trephine here, and penetrated into a cavity large enough to receive the end of the finger. There gushed out a quantity of matter, perhaps a drachm, or more.

The inner surface of the cavity was exceedingly tender, so that he could not bear the introduction of the finger, or even of a probe. On the following day there was a good deal of inflammation in the neighbourhood of the part in which the operation was performed; in the course of a few days an abscess formed, which burst externally just below the ankle, and then the inflammation subsided. The opening made by the trephine became filled up with granulations, and the wound healed favourably. This took place many years ago; I have seen the patient every now and then since, and he has continued perfectly well.

I have had two cases of this kind under my care in this hospital. One was a boy, who had a considerable enlargement of the lower end of the tibia, attended with a great deal of pain. I trephined the bone, and let out nearly half an ounce of matter. The other was a man, whose case I will give you a little more in detail. His name was Mowbray, and he was admitted in October 1838, being then 24 years of age. He had an enlargement of the upper end of the tibia, extending to the distance of $2\frac{1}{2}$ inches below the knee. The circumference of the leg at this part was about an inch more than that of the leg of the other side. The skin over the enlarged bone was tense, and there was a blush of dark redness on the inside. He said that six years ago there took place some enlargement of the head of the tibia, attended with a dull pain. Leeches were applied, and some other treatment was had recourse to; I know not what. The pain continued for about six months, it then subsided, and he became quite free from it, until about three months before he came to the hospital, when it returned, and the bone began to enlarge. The pain at the time of his admission was so severe that he could not sleep at night. It affected his health; he had lost flesh, and could take little or no food. I concluded that there was probably an abscess in the tibia, but as the disease had only been of short duration, I thought it might be better to treat it as if it were merely chronic inflammation in the first instance, having recourse to some other remedies before I performed the operation. I prescribed, therefore, calomel and opium, sarsaparilla (p. 1401), and iodide of potassium, one after the other. At last, there being no amend-

ment, I applied the trephine at that spot where the bone appeared more tender than elsewhere, and thus exposed an abscess, which contained two or three drachms of pus. The relief was immediate, and soon afterwards the patient left the hospital cured.

I will mention another case. In the year 1841, a young lady came to consult me on account of pain in the lower end of the tibia. It began in the spring of 1835, when she had an attack of what appeared to be inflammation of the bone. The pain was at first confined to the lower end of the tibia, but afterwards she had, in addition to it, other pains, apparently of a nervous character, extending up the limb to the hip. She was of an hysterical constitution, which might, perhaps, make the diagnosis of the disease a little more difficult, the hysterical pain being mixed up with the other. However, I found her having occasional attacks of most severe pain in the lower end of the tibia, the bone being enlarged and tender to the touch; and, after a most careful examination, I was satisfied that there must be an abscess in the bone. Accordingly, I recommended the application of the trephine. She could not then stay in town, and, either because her surgical attendant in the country did not accord with me in opinion, or because she would not submit to it, the operation was not performed. She dragged on a very uncomfortable existence for four years more. In the interval she was married, travelled abroad, had various opinions, tried different remedies both here and elsewhere, but nothing afforded her any relief. Last August she again came under my care: the tibia was then very much enlarged; at times she was quite free from pain, at other periods she had severe attacks of it, so that she could not sleep at night. I was still of opinion that there was a collection of matter within the tibia. Mr. Travers and Mr. Key saw the patient with me, and it was agreed that I should perforate the bone with the trephine. Accordingly I performed the operation. The bone was excessively vascular, so that there was a good deal of bleeding; and, towards the end of the operation, a quantity of what appeared to be sero-purulent fluid gushed out from beside the trephine, mixing with the blood. At the

bottom of the bone removed by the instrument there was a cavity that would just receive the end of the finger, and from which the fluid had escaped. After this she had considerable pain for some time, but evidently of an hysterical character. She went into the country, and I have been just informed that the wound has been for some time healed, and that she is free from all her former symptoms. The piece of bone that was taken away is upon the table; it is more hard and compact than it ought to be just above the ankle, where, in the natural state, there is a more cancellous structure. You will perceive on its under surface, one corner of the cavity in which the sero-purulent fluid was lodged.

Since I first published some observations on the subject, in the year 1832, I have the satisfaction of knowing that similar cases have been treated successfully in the same manner by other surgeons. Mr. Liston has given me an account of two such cases, which occurred in his practice, and I have in my possession the written statement of a third one, in the hospital at Lincoln.

Now what are the circumstances that would lead you to suspect the existence of abscess in the tibia? and supposing it to be probable that such an abscess exists, how are you to proceed to relieve it?

When the tibia is enlarged from a deposit of bone externally—when there is excessive pain, such as may be supposed to depend on extreme tension, the pain being aggravated at intervals, and these symptoms continue and become aggravated, not yielding to medicines or other treatment that may be had recourse to—then you may reasonably suspect the existence of abscess in the centre of the bone. You are not to suppose that there is no abscess because the pain is not constant; on the contrary, it very often comes on only at intervals, and in one of the cases which I have related there was, as I then mentioned, an actual intermission of seven or eight months. After the disease has existed a certain number of years, indeed, the pain never entirely subsides, but still it varies, and there are periods of abatement and of exacerbation. The combination of circumstances which I have described will fully justify you in making an opening into the bone

with a trephine. But how will it be if you are mistaken? This will not often occur, but if it should, really the taking out of a circle of bone can be of no consequence; no injury follows the operation—it is unattended with danger. The operation is a very simple one. You expose the surface of the bone, and make a circular opening, with a trephine at that part where there seems to be some tenderness and some pain on pressure. One principal thing to be attended to is that you have a proper trephine. You do not want so large a one as for the cranium, and it must be some what differently constructed. Those which lie on the table are made for the purpose. One is of very small diameter, but generally it is quite sufficient. The common trephines are made with a rim or shoulder, and if there be much enlargement of the bone, they will not penetrate deep enough to reach (p. 1402) the abscess. It is true that you may break away the bone afterwards, by means of a chisel, but the operation may be more easily performed with a trephine having no shoulder: which will at once penetrate to the abscess, however deep it may be, and render the chisel unnecessary. The after-treatment is as simple as possible. There may be some pain for a day or two, and especially, as in the case I last mentioned, if the patient be an hysterical female, there may be hysterical pain afterwards; but all that is required is to maintain the general health, and lay on simple dressing; the bone soon granulates, the space is filled up by a sort of fibrous substance, and the wound cicatrises.

But what would happen if you were not to perform the operation? The patient may continue in torture, as I have already told you, for eighteen years, losing all the best part of his life; or a worse event than that may take place. The preparation which I show you is one of the oldest in the Museum. I attended a patient who laboured under various diseases; there were tubercles in the lungs, and vomicae; dead bone in the ribs and some other local complaints which I forget. Besides all this, he had an enlargement of the lower end of the tibia, attended with excessive pain—pain, indeed, hardly to be borne, and which came on in paroxysms lasting for many hours, and then in some degree subsiding. By and by an abscess appeared externally, in the

neighbourhood of the enlarged tibia, and then the pain ceased. Under this complication of disease the patient sank, and died; and on examining the body I found an abscess in the centre of the tibia. One effect of the abscess had been to cause absorption of the cartilage on the ankle-joint. It might have made its way into the joint, but it took another course; and if you examine the preparation, you will perceive on one side of the tibia a round aperture, by which the matter escaped, and by which the external and internal abscesses communicated with each other. It is plain from this, that such an abscess cannot exist for many years without the joint being endangered. In the year 1830, a young gentleman, about thirteen years of age, came under my care. He had just returned from Paris, where he had had an attack of inflammation of the bone and periosteum of the tibia, for which he had been under the care of the late Baron Dupuytren. The inflammation terminated in necrosis. I removed some portions of dead bone, others exfoliated without any operation, and for three or four years pieces of bone continued to come away, none of large size. Among the sinuses that were open, there was one a little below the knee-joint; I could not ascertain whether bone had come from it or not, but it closed and the patient appeared quite well. In the year 1835 or 1836, however, I was consulted by him again, on account of some pain in the upper end of the tibia. Whenever he walked, the knee-joint swelled becoming full of fluid. I applied a splint, kept him quiet, and he seemed quite to recover. I then left off the splint, and allowed him to walk about as usual. The result was, that in the course of two or three days the knee was again filled with synovia. On a blister being applied, the fluid was again absorbed, then reappeared again on exercise. Taking these circumstances into account, and remembering that there had been pain for some time in the upper end of the tibia, and formerly a sinus leading to the centre of the bone, I thought it very probable that the knee-joint was only occasionally affected in consequence of some disease in the neighbouring portion of the tibia. Mr. Keate and Mr. Liston saw the patient with me, and agreed in the opinion that it would be prudent to perforate the head of the tibia with a trephine.

Finding, as well as I could, the most tender spot, I performed the operation, and out gushed three or four drachms of matter. There was no pain afterwards; the wound gradually contracted and healed, and now, when the patient walked, there was no swelling of the knee. The operation was performed in 1837, and I have seen the patient occasionally ever since, and know that he has had no return of the complaint. But is it possible to doubt that, if the state of things I have described had gone on, the knee-joint must have been destroyed? What would have happened if recourse had not been had to the operation? A case occurred in this hospital, not exactly similar, but sufficiently so to enable me to answer this question. A man of the name of Hendrow was admitted, in February 1837, with the upper end of the tibia enlarged just below the knee-joint. There was an opening leading down to the centre of the bone, and a probe passed into it came in contact with a piece of bone that appeared to be dead and loose, so that it was plain that a piece of bone in the centre of the tibia had exfoliated and formed an abscess, which had afterwards made its way externally. But that which renders the case interesting as connected with the present inquiry is this, that whenever the patient took exercise there was an accumulation of fluid in the knee-joint, just as in the last case. The swelling disappeared on the joint being kept quiet; and the motion of the joint was perfect, or nearly so. It seemed plain that there was a piece of dead bone in the centre of the tibia, which was somehow or other doing mischief to the knee-joint. The course to be pursued was evident. I (p. 1403) applied a trephine so as to enlarge the opening through which the probe had passed; it penetrated into a cavity in which there lay a piece of dead bone, about the size of a horse-beam, which was at once removed. Unfortunately, the poor fellow, whose health had been in a bad state previously, had an attack of erysipelas, and died. I took particular care to examine the knee-joint, and I have the notes of the dissection before me. The whole upper part of the tibia was increased in size from a deposit of seabrous bone on the surface. The cavity from which the dead bone had been extracted was of the size of a large cherry, had a smooth internal surface, the bone

around it being somewhat harder than natural. From this a sinus extended up to the knee-joint, and opened into it just at the anterior part of the spine of the tibia. There was no suppuration in the joint. The cartilage covering the head of the tibia in some places remained perfect, but only in narrow stripes; in other parts it had degenerated into a substance something like condensed membrane; in others the only vestige of it was a thin membranous substance—so thin that you could see the bone through it; and in others the bone of the tibia was completely exposed, but not carious. The bone of the tibia was harder and more compact than under ordinary circumstances. It was curious that the condyles of the femur had suffered also, though in a different manner. The bone, instead of being harder, was softer than natural, so that you might cut it with a knife. The cartilage adhered imperfectly to the bone; it could be peeled off, and in some places it had begun to ulcerate. The softening of the condyles of the tibia I have no doubt was the consequence, and not the cause, of the disease; for you will observe that all bones in a state of inaction lose a great part of their phosphate of lime. After compound fracture, when the patient has been long confined, the bone will actually become as soft as a scrofulous bone, so that you may cut them with a knife.

The three last cases show that it is not safe to leave an abscess in the lower end of the extremity of the tibia beyond a certain time; that the joint is always in danger, and that the perforation of the bone is the only remedy. Even if you were mistaken in your diagnosis no harm can arise under certain circumstances from taking away a piece of bone, where there is chronic inflammation in it, even though there be no abscess. The following very remarkable case will illustrate this last observation. A young gentleman who lived at Brixton, was brought to me by Mr. Crowdy, a practitioner of that place, with violent pain in the middle of one arm, the bone itself being enlarged in that part to which the pain was referred. Some remedies were tried, which I need not enumerate, without any benefit. The pain continued, and I began to suspect that there might be an abscess in the centre of the bone. Under this impression I proposed cutting

down upon it, and making an opening with the trephine, so that I might remove the matter, if there were any there. The operation was performed; the trephine penetrated to the centre of the bone, but no matter escaped. I persevered, but still there was no matter, and at last the instrument penetrated completely from one side of the bone to the other. The bone was very hard and compact, and it was as much as the trephine would do to run it through. I thought that I had made a blunder, and that there being no abscess the operation would not be attended with any benefit. The next morning the patient had an attack of pain almost as severe as before the operation, but it did not last long, and he never had any pain afterwards. The wound healed, the relief was completely, and I heard of the patient not long ago as having continued well. I presume that this was a case of chronic inflammation of the humerus, and that taking out the piece of bone from the centre, probably partly by relieving the tension, and partly by a discharge of matter from the bone, unloading the vessels, accounted for the relief which the patient obtained from the operation.

THE END



Brodie's Disease of Joints

Further Observations on the Diseases Which Affect the
Synovial Membranes of Joints

BY

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I

DURING the last session I had the honour of presenting to the Society an account of several cases, which appeared to throw light on the pathological history and classification of the diseases of the human joints. In the present paper, I propose to communicate some brief practical observations on the symptoms, by which those diseases, which affect the synovial membranes, are to be distinguished, and on the treatment, which should be adopted for their relief. On the latter subject indeed, what I have to offer may seem to have little or no claim to the merit of novelty. The effects of the various methods of treatment (p. 240) now employed by physicians and surgeons are for the most part of accidental discovery. The improvement of scientific pathology seldom leads to the invention of new remedies; but it enables us to understand better the application of those, which are already in use; to know the particular cases to which particular remedies are suited, and to distinguish the curable diseases, from those, in which a cure cannot be effected.

II. On the causes and symptoms of inflammation of the Synovial Membrane

Inflammation of the synovial membranes may occur as a symptom of a constitutional disease, where the system is affected by rheumatism; where mercury has been exhibited improperly, or in large quantities, or where there is general debility from any other cause. But in these cases, the inflammation is seldom severe; it occasions an effusion of fluid into the joint, but rarely terminates in the extravasation of coagulable lymph, or thickening of the inflamed membrane. Sometimes it leaves one joint to attack another, or it suddenly subsides without another joint becoming affected.

At other times the inflammation occurs as a local affection produced by a sprain, the application (p. 241) of cold, or arising from no evident cause. It is here for the most part more severe, and of longer duration: it leaves the joint with its functions more or less impaired, and occasionally terminates in its total destruction. In itself it is a serious disease, but it is often confounded, under the general name of white swelling, with other diseases, still more serious. In some cases, it assumes the form of an acute, but in the greater number of instances, it has that of a chronic inflammation.*

In the former, there is pain and tenderness of the joint, and usually redness of the skin. The pain is severe; not referred to a particular spot, but to the whole joint. When the pain has existed for some time, swelling takes place. The period at which the swelling shews itself, varies from a few hours, to two or three days, from the commencement of an attack. The patient usually keeps the limb a little bent, and every attempt to bend or extend it further aggravates the pain. (p. 242) With these symptoms,

* It is to be observed, that the boundaries of acute and chronic inflammation in these, and in other cases, are not well defined. These terms accurately enough express the two extremes, but there are intermediate degrees of inflammation of which it is difficult to decide, whether they should be considered as being of the acute or chronic kind. Language can not supply names for all the varieties of morbid action which occur, but the surgeon will learn to distinguish them, and the corresponding varieties of treatment, and it is this nicer discrimination which forms a principal difference between the experienced and inexperienced practitioner.

there is inflammatory fever. In a few days the disease either subsides altogether, or assumes the chronic form: more frequently it has this form from the beginning.

Where there is chronic inflammation of the synovial membrane, the pain and tenderness are less, so that the patient is able to walk about, and often without experiencing any severe distress. There is no unusual redness of the skin, and little or no fever. The swelling begins soon after the commencement of the attack, but it increases less rapidly than where the inflammation is acute. These symptoms vary in degree at different periods, and generally are aggravated by exposure to cold or any unusual exertion.

In the first instance, the swelling of the joint arises entirely from a preternatural quantity of synovia being collected in its cavity. In the superficial joints, the fluid may be distinctly felt to undulate, when pressure is made alternately by the two hands placed one on each side. When the inflammation has existed for some time, the fluid is less perceptible than before, in consequence of the synovial membrane having become thickened, or from the effusion of lymph on its inner or outer surface; and in many cases, when the disease has been of long standing, although the joint is much swollen, and the symptoms of inflammation still exist, the fluid in its cavity is scarcely to be felt. As the swelling consists more of solid substance, so the (p. 243) natural mobility of the joint is in a greater degree impaired.

The form of the swelling deserves notice. It is not that of the articulating ends of the bones, and therefore it differs from the natural form of the joint. The swelling arises principally from the distended state of the synovial membrane, and hence its figure depends in great measure on the situation of the ligaments and tendons, which resist it in certain directions and allow it to take place in others. Thus, when the knee is affected, the swelling is principally observable on the anterior and lower part of the thigh, under the extensor muscles, where there is only a yielding cellular structure between those muscles and the bone. It is also often considerable in the spaces between the ligament of the patella and the lateral ligaments, the fluid collected in the cavity causing the fatty substance of the joint to protrude in this

situation, where the resistance of the external parts is less than elsewhere. In the elbow the swelling is principally observable on the posterior part of the arm, above the olecranon and under the extensor muscles of the fore-arm; and in the ankle it shews itself on each side, in the space between the lateral ligaments and the tendons, which are situated on the anterior part. In like manner in other joints, the figure of the swelling, whether it arises from fluid, along, or joined with solid substance, depends in great measure on the ligaments (p. 244) and tendons in the neighbourhood, and on the degree of resistance which they afford, and these circumstances, though apparently trifling, deserve our attention, as they enable us more readily to form our diagnosis.

In the hip and shoulder the disease occurs less frequently than in the superficial joints. The effused fluid can not here be felt to undulate, but the swelling is perceptible through the muscles which cover it. When the hip is affected the pain is usually confined to the hip itself; sometimes it is referred to the knee also, as in cases where the cartilages of the hip are ulcerated. The following circumstances enable us to distinguish the two diseases from each other. In the former the pain is more severe in the first instance than afterwards; and there is welling of the nates. In the latter the pain is trifling at first; becomes gradually worse, till it is at last exceedingly severe, and the nates are wasted and flattened instead of being swollen.

After the inflammation of the synovial membrane has subsided, the fluid is absorbed, and in some instances the joint regains its natural figure and mobility; but in the majority of cases stiffness and swelling remain. In the superficial joints the swelling has sometimes the form of the articulating ends of the bones, that is, the natural form of the joint, and we may suppose it in this case to arise (p. 245) from the thickened state of the synovial membrane. At other times it has the same peculiar form, which it possessed while the inflammation existed, and while fluid was contained in the joint, and we may suppose that it depends principally on the inner surface of the synovial membrane having a thick lining of coagulable lymph.

The chronic inflammation of the synovial membrane often

continues for many months, and after having subsided is very liable to recur from slight causes. Thus a person has this disease in his knee; the inflammation is cured, but tumor and stiffness remain. Whenever he is exposed to cold, or exercises the limb in an unusual degree, and often without any evident reason, the pain returns and the swelling is augmented. Such cases are of frequent occurrence, and they form a large proportion of those which are known by the name of white swelling.

Long continued and neglected inflammation of the synovial membrane occasionally terminates in the formation of an abscess in the cavity of the joint, in ulceration of the cartilages, and in complete destruction of the articulating surfaces. In this last stage, if we wish to know whether the inflammation of the synovial membrane, or the ulceration of the cartilage, has been the primary disease, we must form our judgment, not from the present symptoms, but from the previous history (p. 246) of the case. It is indeed often difficult to procure a history, on the accuracy of which we can rely, particularly in hospital practice; but this is of less importance, as whatever the disease may have been in its origin, where it has proceeded so far as has been described, there is no difference with respect to the treatment; and in general, no remedy can be employed with any prospect of advantage, except the removal of the limb by amputation.

III. On the Treatment of the Inflammation of the Synovial Membrane

In the acute form of the disease, leeches may be applied to the part; and in most instances it will be right to take blood from the arm. Warm fomentations produce better effects than cold lotions. Attentions should be paid to the state of the bowels, and Dover's powder, or some other diaphoretic medicine, may be exhibited. Under this treatment the acute inflammation in general speedily subsides.

The chronic inflammation is relieved more slowly. In the first instance, the joint should be kept in a state of perfect rest. Blood should be taken from the part by means of leeches or cupping, and this may be followed by the application of a blister,

(p. 247) large enough to include the greater part of the circumference of the joint. Under this treatment the pain is relieved, and in a few days the swelling, as far as it depends on the fluid collected in the cavity of the joint, is much diminished. Even where the tumor is solid, arising from the effusion of coagulable lymph, it will in a great degree subside, and sometimes be entirely dispersed, provided the lymph has not yet become organized. A single blister often produces marked good effects, but it is generally necessary to repeat both the blister and the blood-letting several times. The repeated application of blisters is more efficacious than a single blister kept open by the savine cerate, or by other means, for a considerable time. When the inflammation is in a great measure subdued, a moderate degree of exercise of the joint is rather beneficial than otherwise. Liniments, which irritate the skin, may be rubbed on twice or three times in the day. The following liniment is more stimulating than those in common use, and has appeared to me in most instances to have been productive of much better effects with respect to the disease.

Olei Olivae oz. iss.

Acidi Sulphurici oz. fs. M. fiat linimentum.

It may be used of this strength for the class of persons, who apply at an hospital for relief; but for persons of a higher class in society, in whom (p. 248) the cuticle is thinner, and the cutis more easily irritated, the proportion of the olive oil should be greater. The effect of this liniment is to excite some degree of inflammation of the skin; the cuticle becomes of a brown colour, and separates in thick, broad scales, and the inflammation of the internal parts is relieved, probably on the same principle as by a blister. The friction used in applying the liniment appears to be of service after the inflammation is nearly subdued, but if friction be employed in the first instance the disease is aggravated.

No other remedies seem to be productive of much benefit.

Issues and setons, which are useful in cases of ulceration of the cartilage, are of no service whatever in this disease.

Plasters of gum ammoniac, and others of a similar nature, are

of little efficacy, while inflammation still exists; but afterwards they are of use in guarding the joint from the influence of the external cold, and preventing a relapse.

The swelling and stiffness that remain after the inflammation has subsided, if moderate in degree, may be relieved by the free exercise of the limb, and by friction. The mercurial ointment with camphor may be rubbed on the joint; or friction (p. 249) may be made by the hand with starch or other fine powder. The friction however should be employed with caution, as, when used too freely, it sometimes occasions a return of the inflammation. Whenever there is the slightest indication of this being the case, the friction should be omitted for a time, and leeches should be applied, and if the friction be resumed it should be employed in a less degree, and less frequently than before.

When the swelling and stiffness in consequence of the inflammation are very considerable, I have seldom known much, and I have never known entire relief produced by friction or by any other means. Here too the patient is more liable to a return of the inflammation, and hence friction must be employed with still greater caution than in other cases.

On the whole I have not found so much good produced by friction, as from what I had heard of its effects, I had been led to expect; and I have known it, when used too freely, or too early in the disease, to delay rather than to expedite the cure. Friction appears to be more efficacious where the stiffness of a joint depends on a contracted state of the muscles or tendons of the limb, and on these being glued to each other and to the surrounding parts, than where it is the consequence of disease in the joint itself.

(p. 250) I have in several instances tried the effect of pumping hot water on a stiff joint, as recommended by Le Dran, and as now practised at some watering-places. The blow of a column of water falling from a height of several feet produces considerable friction, with which are combined the relaxing powers of heat and moisture. This practice is certainly productive of benefit; but the observations just made apply to this as well as to the other modes of producing friction.

IV. On the Symptoms produced in those Cases, in which the Synovial Membrane has undergone a morbid Change of Structure

In my former communication respecting the diseases of the joints, I gave an account of several cases, in which the synovial membrane had undergone a peculiar morbid alteration of structure. The observations which I then made have been fully confirmed by many similar cases which have since come under my notice. This disease generally takes place in young persons under, or not much above, the age of puberty. I do not recollect more than one instance of it having occurred after the middle period of life. In general it can be traced to no evident cause; but occasionally it takes place as a consequence of repeated attacks of inflammation. In this respect it resembles other diseases of the same order. Inflammation of the lungs may produce tubercles, and inflammation of the breast may occasion the growth of a schirrous tumor. Where I have had an opportunity of examining the morbid appearances after amputation, I have always found the whole, or nearly the whole of the synovial membrane affected by the disease; but it is probable, that if the examinations were made at an earlier period, we should always find the morbid change originating in some one point. A patient was admitted into St. George's Hospital in whom this disease was beginning on the inside of the knee: from thence (in the course of three months) it gradually extended itself in every direction over the whole circumference of the joint. In a girl, who laboured under this affection of the knee, but who died in the hospital of another complaint, I found one-half of the synovial membrane in a state of disease, and the other half retaining its natural structure and appearance.

In the origin of this disease there is a slight degree of stiffness and tumefaction, without pain, and producing only the most trifling inconvenience. These symptoms gradually increase; at last the joint scarcely admits of the smallest motion, the stiffness being greater than where it is the consequence of simple inflammation. The form of the swelling bears some resemblance to that in cases of inflammation of the synovial membrane (p. 252), but it is less regular. The swelling is soft and elastic, and gives

to the hand a sensation as if it contained fluid. If only one hand be employed in making the examination, the deception may be complete, and the most experienced surgeon may be led to suppose that there is fluid in the joint, when there is none; but if both hands be employed, one on each side, the absence of fluid is distinguished by the want of fluctuation.

The patient experiences little or no pain until abscesses being to form, and the cartilages ulcerate; and even then the pain is not severe, as where the ulceration of the cartilages occurs as a primary disease, and the abscesses heal more readily, and discharge a smaller quantity of pus than in cases of this last description. At this period the patient becomes affected with hectic fever; loses his flesh, and gradually sinks, unless the limb be removed by an operation.

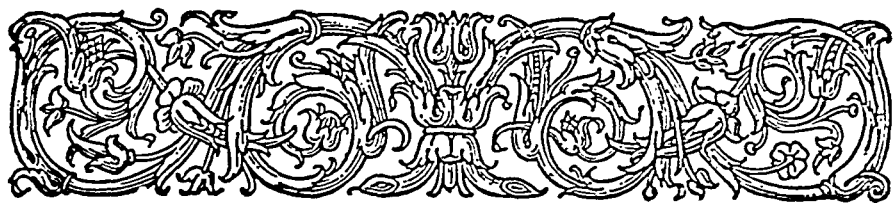
The progress of this disease varies in different cases. In general one or two years elapse before it reaches its most advanced stage; but sometimes the period is much longer; and occasionally it becomes indolent, so that it remains during many months without any sensible alteration. In like manner tubercles of the lungs, or schirrus of the breast in some instances remain in an inactive state for several months, or even for some years.

(p. 253) The diagnosis of this disease is seldom difficult. The gradual progress of the enlargement and stiffness of the joint without pain; and the soft elastic swelling without fluctuation, in most instances enable us to distinguish it, not only from inflammation of the synovial membrane, but also from the other morbid affections to which the joints are liable.

V. On the Treatment of Cases, in which the Synovial Membrane has undergone a morbid Alteration of Structure

Where there is welling and hardness following inflammation, the substance which has been effused may be absorbed, and the swelling and hardness may disappear, but I know of no instance in which an organ having completely lost its natural structure is capable of having that structure restored. Physicians and surgeons have been employed during successive ages in endeavour-

ing to discover a cure for tubercles of the lungs, and cancer of the breast, and the result of their labours is only to prove that these diseases are incurable. Analogy therefore would not lead us to be sanguine as to the discovery of a remedy for this disease of the synovial membrane, and experience shews that it is equally incurable with other maladies of the same order. By means of rest and cold lotions the progress of the disease may (p. 254) be somewhat checked, as suppuration of tuberculated lungs may be retarded by occasional bleeding, and a milder climate; but ultimately the ulceration of the cartilages, the formation of abscess in the cavity of the joint, and the consequent disturbance of the general health, render the amputation of the limb necessary in order to preserve the patient's life. At this period therefore the surgeon is called upon to recommend, and to urge an operation; but at an earlier period it is a matter of choice with the patient, whether he will live with the incumbrance of an useless limb, till the advanced stage of the disease renders its removal indispensable, or whether he will submit to the loss of it before the absolute necessity for losing it exists.



Brodie's Pile

Lectures on Diseases of the Rectum

BY

SIR B. C. BRODIE, BART.

Lecture III. Preternatural Contraction of the Sphincter Ani

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THE orifice of the anus, as you know, is closed by the sphincter muscle. The ordinary condition of this muscle is that of being contracted, and thus it prevents the involuntary discharge of feces from the rectum. In the expulsion of the alvine evacuations, the effort of the abdominal muscles and diaphragm is always attended with a relaxation of the sphincter muscle, in consequence of which the contents of the bowel are allowed readily to escape. If this consent and sympathy between these different muscles did not exist—the whole of them being in a state of contraction at the same time—the feces would be expelled with very great difficulty and distress to the patient, or not at all. Now it happens that this state of things sometimes actually exists, and the result is precisely what I have mentioned. The contraction of the sphincter at first appears to be merely spasmodic, without any other change of its condition; but you know, that in proportion as muscles are called into greater action, so they become increased in bulk; and, in conformity with this general rule, when spasmodic contraction of the sphincter muscle has existed for a long time, the muscle

becomes considerably larger than it was in its natural state before the disease existed.

This disease is not of uncommon occurrence. It is met with chiefly in women, especially those who are disposed to hysteria. It is, however, met with in other women, and sometimes in the male sex.

The patient, under these circumstances, is forced to strain very much in passing her evacuations; and this is especially the case when the feces are hard, or even solid. There is pain not only when the feces are being passed, but for a very considerable length of time afterwards; and in some cases the pain will remain from the period of one alvine evacuation to that of another; so that it is constant, or nearly so. It is remarkable what misery some persons suffer under the circumstances which I have just described.

In connection with spasmodic contraction of the sphincter muscle, you will frequently find a small ulcer of the mucous membrane of the rectum. This ulcer is always in a particular spot, at the posterior part, opposite to the point of the os coccygis. I imagine that it arises from the mucous membrane there being torn by the pressure of the hard feces, at the time that the evacuation is labouring, as it were, to get through the contracted orifice of the anus. Such an ulcer as I have just described adds very much to the patient's sufferings; it is always excessively sensitive; the least pressure of the finger upon it occasions the greatest pain, and the pressure of solid feces produces the same effect.

An ulcer of this kind is met with in some cases independently of disease of the sphincter muscle; but to that I shall advert hereafter.

Treatment.—When the patient does not suffer excessively from this disease, you may sometimes relieve her in the following manner: Give her purgative medicine, so that she may never have hard or figured evacuations, and let an opiate suppository be introduced at night. I have formerly used a suppository with extract of belladonna, with manifest advantage; but I owe that I am not in the habit of frequently employing this remedy. Even (p. 27) used in the form of a suppository, the belladonna sometimes produces very serious symptoms, by its influence on

the brain. In addition to what I have mentioned, the patient may introduce a bougie into the anus, to dilate the orifice of the bowel, each time before she goes to the water-closet.

These remedies, however, are of no avail in bad cases of this disease; and then it is absolutely necessary to resort to some more certain means of cure. It may always be relieved by a simple operation—the division of the sphincter ani muscle. You introduce a straight probe-pointed bistoury into the anus, and cut through the fibres of the muscle, taking care not to penetrate beyond them. The fibres are of considerable thickness, and you cannot cut them through at one incision, nor should you attempt it; the knife must be drawn across the muscle two or three times before the operation is completed. It is generally sufficient if you divide the muscle on one side. It is better to divide it laterally than either in the posterior or anterior direction. The wound does not readily heal if the division be made towards either the perineum or the os coccygis; nay, more than that, if in the female you divide the muscle towards the perineum, and consequently towards the vagina, you make the patient miserable for life, for there is incontinence of *fæces* ever afterwards; whereas, if you divide it in any other direction, this inconvenience is altogether avoided after the wound is healed.

The operation of dividing the sphincter muscle is not very painful, except in those cases where the disease is complicated with ulcer at the back part of the rectum; neither is there ever any hæmorrhage of consequence, as the pressure of the finger, or a plug of lint, will always command it. The relief is immediate; and the very next time that the patient has an evacuation, there is an end of all the pain and difficulty which she suffered before. It is better, however, that she should not have an evacuation immediately after the operation, and therefore I generally give her an active purgative on the preceding day, and some opium afterwards to keep the bowels constipated. After two or three days castor oil may be exhibited, and the bowels opened. The wound requires very simple treatment; a little dressing of lint may be applied to it till it is cicatrized; and cicatrization is generally completed in about three weeks.

No inconvenience whatever follows the division of the sphincter

muscle, except it be made, as I have mentioned, in the female, in the direction forwards. The patient retains her fæces as well as ever, and yet the difficulty of voiding them is relieved. All the symptoms, so far as I have seen, are permanently removed. I have performed this operation of dividing the sphincter muscle for this disease, and in other cases, a great many times; and I have been accustomed to say that it is an operation free from danger; but, after all, there is no operation in surgery, not even the slightest, of which we can assert this as a general proposition, or as one to which there are absolutely no exceptions. The utmost that we can venture to say is, that the probability of any bad result is so small, that we ought not to calculate on it; and that if we were to calculate on such chances in the common affairs of life, we should do nothing. I have known two instances of persons dying after the extraction of a tooth; I have known others die in consequence of being bled in the arm, or of erysipleas occurring after being cupped. I have known the bite of a leech, and the sting of a wasp, and the prick of a pin, to prove fatal; and I have lately had the misfortune of losing a patient after the division of the sphincter ani muscle. The case occurred in a lady of a peculiarly susceptible nervous system. Immediately after the operation she fell into what might be called a state of hysterical syncope, from which she did not recover until after the lapse of three or four hours. She died at the end of a week, with inflammation of the pleuræ and peritonæum, which had caused a very large effusion of turbid serum into the cavities of the chest, and a smaller effusion into that of the abdomen also. There was no inflammation of the rectum, nor of the cellular membrane or other textures in immediate connexion with it; and it was evident that the pleuritic and peritonæal inflammation had not extended from the part on which the operation had been performed, but that it had been the result of the impression made on the system generally. I cannot so well compare the case to any thing, as to one of puerperal fever.

ULCER ON THE INSIDE OF THE RECTUM

The ulcer which occurs in connexion with a contracted sphincter muscle, in some instances exists independently of it. You may

discover it on the posterior part of the rectum, opposite to the point of the os coccygis; and, as I have already stated, it occurs, for the most part, in persons who have costive bowels and hard stools, the mucous membrane being under these circumstances lacerated by the pressure of hard evacuations. When once produced, the ulcer is very difficult to heal, and very frequently it goes on spreading till it becomes of considerable size. It is a superficial ulcer, of exquisite sensibility, and (p. 28) great pain is always produced by the passage of the fæces over it, lasting for a considerable time after each evacuation. In some instances, considerable hæmorrhage takes place from an ulcer of this kind.

Treatment.—The ulcer is always cured by a division of the sphincter muscle. This, however, is not always necessary, unless the muscle be actually contracted. Mr. Copeland has observed, that when there is a simple ulcer, the mere setting of the mucous membrane at liberty, by dividing it longitudinally, so as to include the ulcer in the incision, is sufficient to effect a cure. I have known this to succeed in several instances, and I believe that it is Mr. Copeland's ordinary practice. However, a cure may be obtained, in many instances, without an operation of any kind, by means of the conf. piperis compos, or Ward's paste, given internally (the bowels being at the same time kept gently open by the use of lenitive electuary and sulphur, or some other simple aperient). Ward's paste may be applied locally also. I had a case, not long since, in which the patient was unwilling to submit to the division of the mucous membrane, and where she got well under the use of suppositories of Ward's paste and soap. A piece of this, blended with soap, was introduced into the rectum twice a-day, gentle aperients being exhibited at the same time, so as to prevent her having hard evacuations.

STRICTURE OF THE RECTUM

Under the appellation "stricture of the rectum," various diseases have been confounded with each other—some malignant, and some not malignant; but I am going to speak now of that stricture or contraction of the gut which does not partake of a malignant character. Malignant diseases of this organ will be considered in another lecture.

Here is a specimen [presenting it] of stricture of the rectum. On dissecting a case of simple stricture of the rectum, I have found the mucous membrane thickened, of a harder structure than natural, and the muscular tunic thickened also. The stricture sometimes occupies the whole length of the gut, for some way up above the anus—perhaps three or four inches, as in the specimen just shewn you; at other times it is only of short extent. Frequently the gut is of its natural diameter close to the anus, and about an inch and a half or two inches above it there is a circular contraction, and then above that the gut is of its natural diameter again. Although the contraction may occupy only a small portion of the length of the rectum, yet the disease of the tunics is generally more extensive. Thus, if there be a contraction of the gut two inches above the anus, you find the mucous membrane between the stricture and the anus thickened, and in an unhealthy state; and on passing the finger through the stricture into that portion of the gut above it, you will find the mucous membrane in this situation in an unhealthy state also.

The disease occurs in either sex: in adult persons more than in children. It comes on gradually. The patient finds a little difficulty in passing the evacuations; then the difficulty becomes greater; he is forced to strain when at the water-closet, especially if the fæces be hard; and at the same time the fæces are observed to be of a very small diameter. The constant straining against the stricture causes the diseased part to become inflamed, and then the evacuation is attended with a great deal of pain, there being also a discharge of mucus constantly dribbling from the anus, and staining the patient's linen of a brown colour. As the disease advances, some parts of the mucous membrane ulcerate. This causes the pain to be much aggravated, there being then a discharge not only of mucus, but of blood and pus from the anus. If the disease proceeds still farther, inflammation takes place in the cellular membrane around the gut; putrid abscesses form, which burst in various situations at every side of the anus, into the urethra in men, and occasionally in women into the vagina. These abscesses are probably formed in the following manner:—ulceration takes place of the mucous membrane, and of the muscu-

lar tunic of the gut, in consequence of which a very small communication is formed between the cavity of the rectum and the cellular membrane in the neighbourhood; then some small portion of the contents of the bowel escapes into the cellular membrane, inducing inflammation and suppuration, the admixture of a little fæculent matter causing the contents of the abscess to be putrid. In some instances the patient dies with symptoms of strangulated hernia—that is, a piece of hard fæces is lodged above the stricture, and cannot pass through it; thus there is a mechanical obstruction to the passage of the fæces; the belly becomes tympanitic, the tongue dry; there is sickness, vomiting, and the other symptoms indicating strangulation. He may have one of these attacks, and by means of injections, and the use of a bougie, may recover; he may have a second, and recover from that; and then he may have a third, which may prove fatal. In the most advanced stage of this disease, independently of these attacks, the patient suffers much (p. 29) in his general health, loses flesh, perspires at night, his digestion is deranged, he is emaciated and hectic, and thus gradually becomes exhausted.

The progress of the disease which I have thus described in a few words, is, however, lingering and tedious. The patient may die, even where no remedies are employed, after ten or twelve years of inconvenience first, and of suffering afterwards. In some cases, under a judicious treatment, although the disease cannot be cured, it may be much mitigated, and may never prove fatal.

Treatment.—When you are called to a patient with stricture of the rectum, you should first make an examination with the finger, so as to ascertain exactly where the stricture is situated, how high up it extends, and how much of the gut is included in it. If the stricture be not in a very irritable and tender state, the patient may at once derive benefit from mechanical dilatation by the use of a bougie. You will ascertain the diameter of the stricture with the finger as nearly as you can do so, and introduce a bougie, of proper size, through its orifice. The bougie must be allowed to remain in the stricture five or ten minutes, or in some cases for a longer time; and the operation must be repeated every

day, or every other day, according to circumstances. In this manner you will gradually be enabled, in the early stage of the disease—I will not say to restore the gut to its natural diameter—but to dilate the stricture so much that the evacuations may be readily discharged, and that the patient may suffer but little inconvenience from it. I saw not long since a lady respecting whom I had been consulted about three or four years previously. At that time the stricture was so great, that I could introduce only a small urethra bougie. I directed her to commence a course of bougies, which her medical attendant introduced for her. They were very gradually increased in size; and when I last saw her the stricture would admit one of very large diameter; and she experienced no more than the slightest inconvenience from the complaint. Here, as in cases of stricture of the urethra, the use of the bougie must be continued. If it be neglected the stricture will return, and be worse than ever.

In some cases of this disease you may facilitate the process of cure in the following manner. In the cases to which I allude, the stricture is situated about two inches above the anus, and occupies only a small portion of the length of the gut. It forms a circular band, embracing the finger, as narrow as a cord. A stricture of this kind may be divided in two or three parts of its diameter, before you begin the use of the bougie, in the following manner:—Introduce a *bistouri caché*, and let the screw be so adjusted that the blade may be opened about the sixth of an inch, but certainly not more than a quarter of an inch. The *bistouri* must be introduced with the blade shut; then press on the handle, open the blade, and, drawing it out, you nick the stricture first in one part of its diameter, then in another, and then in a third. This being done, a larger bougie may be introduced than could be done before, and the process of cure is very much expedited.

But in a great number of cases where the disease is far advanced (and, generally speaking, you are not consulted till that is the case, especially in hospital practice), you cannot resort to the use of the bougie in the first instance, or, if you do, it must be employed in combination with other remedies. It will be necessary to lessen the irritability of the bowel by the introduction of

an opiate suppository every night, a gentle aperient being taken in the morning. The patient may take a combination of caustic potass with balsam of copaivi; half a drachm of balsam of copaivi, fifteen minims of the *liq. potassæ*, three drachms of mucil. gum arabic, and about nine drachms of carraway water. A draught of this composition may be taken three times a day with very great advantage. Mr. Bryant, a respectable practitioner in the Edgeware Road, two or three years ago recommended to me a decoction of *achillea millefolium*, which I have employed in some of these cases with manifest advantage. About two ounces of the *achillea millefolium* may be put into a pint and a half of water. This may be boiled down to a pint, of which a patient may take a wine glass three times a day. The *achillea millefolium* is sold at the herb shops in Covent Garden; it is not in the Pharmacopœia, although it has been always a popular remedy.

Where abscesses have formed in the neighbourhood of the gut, it is of no service to lay them open. I have told you on many occasions, that if abscesses are connected with diseased structure, they are not likely to heal; and you only make the patient worse by laying them open, there being, of course, a much greater extent of raw surface after the operation than before. If these abscesses are to be healed at all, it can only be after the stricture has been fully dilated.

In some cases the fæces accumulate above the stricture, the bowel in this situation becoming distended into a large bag, forming an immense reservoir of fæculent matter, always pressing against the stricture, and aggravating the disease. It is (p. 30) very important to empty the bowel which is thus loaded; and you can only do it in the following manner:—Introduce an elastic gum catheter through the stricture into the fæculent mass above; inject tepid water, or tepid soap and water, or a weak solution of caustic alkali; and by repeating this operation, and washing out the gut with warm water every day, or every other day, you may at last get the whole of the fæculent accumulation dissolved, and empty the reservoir. When this has been accomplished, the injection of warm water should be constantly repeated, so as to prevent the accumulation taking place again.

In some cases of stricture of the rectum, I have thought that the patient has derived benefit from the application of mercurial ointment to the inside of the gut, which is easily managed in the following manner:—Let the bougie be covered with lint smeared with mercurial ointment: the bougie thus anointed must be allowed to remain in the stricture for a few minutes daily.

Your success in the management of this disease will vary very much in different cases. It will depend chiefly on the period of the disease at which you are consulted. If it be quite in the early stage, you may render the patient great service; and although you cannot cure stricture of the rectum any more than you can cure stricture of the urethra, yet you can dilate it, and keep it dilated, so that the patient will suffer little from it, and that it will not shorten his life. But if you are consulted in the advanced stage, when the stricture is much contracted, when the mucous membrane is ulcerated, when abscesses have formed in the neighbourhood, you can only palliate the symptoms in some degree. The patient under these circumstances, in spite of all your efforts, will lead a miserable life, and in all probability will ultimately fall a victim to the disease.

Strictures of the rectum are commonly situated in the lower part of the gut, within the reach of the finger. Are they ever situated higher up? I saw one case where stricture of the rectum was about six inches above the anus; and I saw another case where there was stricture in the sigmoid flexure of the colon, and manifestly the consequence of a contracted cicatrix of an ulcer which had formerly existed at this part. Every now and then, also, I have heard from medical practitioners of my acquaintance of a stricture of the upper portion of the rectum, or of the sigmoid flexure of the colon, having been discovered after death. *Such cases, however, you may be assured, are of very rare occurrence.* Inquire of anatomists who have been for many years teachers in the dissecting-room, or of surgeons who have witnessed a great number of examinations in the dead-house of an hospital, and they will bear testimony to the correctness of what I have now stated.

Nevertheless, an opinion has of late years prevailed among

some members of our profession, that a stricture high up in the rectum is a very frequent cause of constipation of the bowels; and I have known an almost incredible number of persons who have been treated on the supposition of their labouring under such a disease, by the introduction of long bougies into the bowel. The only evidence of the existence of a stricture in these cases has been, *first*, that there was obstinate costiveness; *secondly*, that a bougie introduced into the rectum could not be made to pass beyond a certain number of inches beyond the anus.

But what is the value of this evidence when compared with that which anatomy affords of the rarity of this kind of stricture? Are there not many causes of a costive state of the bowels besides mechanical obstruction? Will it be always easy, even in the most healthy rectum, to introduce a bougie more than a few inches into it? Although we call the lower bowel the *rectum*, you know very well that it is any thing but a straight gut. Three or four inches above the anus the rectum begins to make flexures, which increase as you trace it upwards, until they terminate in the sigmoid flexure of the colon. These flexures of the rectum differ in different individuals, and even in the same individual at different periods. When a bougie is introduced, be it small or large, it is certain that it will be stopped somewhere or another by one of these flexures; and nothing can be more unphilosophical than to conclude, because a bougie meets with an impediment at the distance of five or six, or eight or nine inches, that this is the result of an organic disease of the rectum, when the natural formation of the parts will sufficiently account for it.

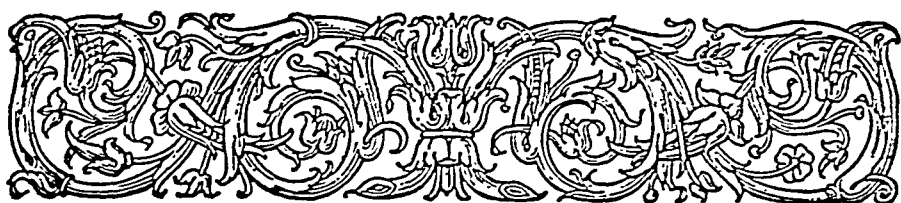
But let us suppose that you actually meet with one of those rare cases in which there is a stricture in the upper part of the rectum; by what means are you to recognize the disease in the living person? Or, if you can recognize it, how can you know its exact situation? If the bougie can only be introduced to a certain distance, how are you to be certain that it is stopped by the stricture, and not by a fold of the bowel, or even by coming in contact with the sacrum?

Further than this, if you employ the force which you would suppose to be necessary (p. 31) to make the bougie penetrate

through the stricture, is there no danger of it penetrating the tunics of the intestine instead? This last is no theoretical objection to the use of these long bougies in diseases of those parts. I will not say that I have seen the patients; but I have been informed on good authority of not less than seven or eight cases in which this frightful accident occurred, and the patients died in consequence.

Taking all these things into consideration, I advise you to lay it down for yourselves as a rule of practice, that you should not use bougies for stricture of the rectum, except where the stricture is within reach of the finger. If there be any exceptions to this rule, they are very rare indeed.

THE END



Brodie's Tumor

Lecture on Sero-Cystic Tumors of the Breast

BY

SIR BENJAMIN BRODIE, BART.

Addressed to the Students of St. George's Hospital, January 21, 1840. Published in
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GENTLEMEN,—Although the pressure of other engagements has caused me to resign my situation as Surgeon to St. George's Hospital, I shall never cease to feel the highest interest in the welfare of an institution to which I am so deeply indebted, nor in that of the Medical School, which is in connection with it, and the advancement and improvement of which has been almost the greatest object of my life, during the last thirty years. Most gladly shall I avail myself of any opportunity which may occur of rendering service either to the one or to the other. I shall always regard the pupils of this school as having an especial claim on my attention, and my best wishes for their success, in the honourable practice of an honourable and independent profession, will attend them through life. In order that I may show that these are not mere words of course, and that what I say is what I really feel and mean, I have offered to the medical officers of the hospital that, if they and you are desirous that I shall do so, I will complete the course of gratuitous lectures which I had begun for the present season; and that I would afterwards deliver an annual course of lectures, also gratuitously, in the theatre of the hospital. This offer has been accepted, and I now proceed to redeem my promise.

But before I go farther, I must explain what these lectures are

intended to be. It is evident that they cannot, as heretofore, assume (p. 809) the form of clinical discourses. At the same time it is desirable that they should be such as will interfere, as little as possible, with the systematic course of lectures delivered by Mr. Hawkins and Mr. Babington. I think that this may be easily accomplished. Not being limited as to the time devoted to a particular subject, I shall be enabled to discuss the history and treatment of the diseases to which I may call your attention at greater length, and more in detail, than can be done on ordinary occasions. I shall sometimes, instead of treating specially of one disease, take a particular symptom, or order of symptoms, as the basis of our inquiries, referring them to the various diseases from which they may arise; and I am much mistaken if this will not enable me to communicate to you some information, which, whatever may be its value in the eyes of a mere morbid anatomist, may prove useful to you when you are first engaged in the practical exercise of your professional duties. I shall, moreover, by means of these lectures, endeavour to supply a considerable deficiency of hospital education. In the wards of the hospital you learn the great principles of disease, and the more important rules of surgery, but you have not the opportunity of learning the whole of what you require to know for the purposes of private practice. Diseases prevail in one class of society which in another are only occasionally met with; and one object which I shall keep in view is that of explaining what might otherwise perplex you when, passing from the bed-sides of the labouring poor, you begin to practice your art among those who live in ease and affluence. In the early part of my professional career it often fell to my lot to experience the want of such instructions, and I am inclined therefore to believe that they will not be unacceptable to you.

The disease of which I propose to treat on the present occasion, is an affection of the female breast. It is one of great interest in various ways, and among others in this, that in its more advanced stages it is liable to be confounded with carcinoma, although it is not really of a malignant nature.' And I may here remark, that it serves very well to illustrate the observations

which I have just made, as I should not have been able to trace its exact history if I had trusted altogether to my hospital experience. In private practice it is of frequent occurrence. Yet I have not met with any description of it in books corresponding to what I have myself observed of its actual progress. You will presently see how this is easily to be explained, by the disease assuming a wholly new character as it proceeds, so that if you were to look at two cases of it, one in an early, and the other in a more advanced stage, without having witnessed the intermediate changes which have taken place, you would be scarcely able to recognise their identity. Let me not, however, be misunderstood as representing that no notice whatever has been taken of it by surgical writers. The account which Sir Astley Cooper has given of the hydatid breast has been taken principally from cases of this disease, and there are also some allusions to it in the *Treatise on Diseases of the Breast*, lately published by M. Velpeau.

The first perceptible indication of the disease is a globular tumor imbedded in the glandular structure of the breast, and to a certain extent movable underneath the skin. Sometimes there is only one such tumor; at other times there are two or three, or many more. The examination of the breast in the living person does not enable you to determine the exact number which exists, as it is only where they have attained a certain magnitude that they are perceptible through the skin. In most instances the disease is confined to one breast, though it is by no means very uncommon for both breasts to be similarly affected.

The globular form which the tumor invariably assumes in the first instance is a sufficient proof that it is formed of fluid collected in a cyst, and of course pressing equally in every direction. If you puncture the tumor with a grooved needle, the fluid may be evacuated to as completely to empty the cyst, and the perfect subsidence of it afterwards proves how little space the cyst itself occupies. The fluid is always serous. When the tumor is small it seems to be serum, unmingled with anything else. In a more advanced stage of the disease, some colouring matter is generally blended with it, and it may be green, or brown, or so dark col-

oured as to be almost black. The quantity of fluid of course varies. In dissection, I have found the cyst to be so small as to contain scarcely a single drop. But it is sometimes capable of containing several ounces. In two cases in each of which I had the opportunity of examining a breast affected with this disease, I found small cysts, composed of a thin membrane, and containing serum, pervading the whole of the glandular structure, the intermediate parts presenting a perfectly healthy and natural appearance, and I could discover nothing more. I am, however, led to suspect that the cysts are originally formed by a dilatation of the lactiferous tubes. In one of the preparations now on the table you will perceive a bristle introduced into the orifice of one of these tubes opening on the nipple, which has passed into a cyst (p. 810) immediately below; and it is not uncommon to find that by pressure on the tumor the fluid may be made to escape by the nipple, even so as to expel the whole of it.

To complete this history of the disease, as it first shews itself, I may add that the general health is unaffected, and that the patient complains of no pain, unless it be that, in some instances, there are those disagreeable nervous sensations which are apt to arise whenever the attention is anxiously directed to any one part of the body. I have never known the disease to occur previously to the age of puberty, nor after the middle period of life: and, if I am not much mistaken, it is more common in single than in married women.

There are not a few cases in which no morbid changes take place beyond that which I have already described; the cysts remaining unaltered, or only slowly increasing in size during the remaining of the patient's life. But in other cases the tumors lose their globular form, and a solid substance is deposited in the breast, connecting different cysts with each other in one large mass of disease. This process may be going on for many successive years without inducing pain or much inconvenience, except what belongs to the bulk of the tumor. But the period at last arrives when other changes take place, the disease assuming a more formidable and dangerous character. The skin, in some one part, more tense and thin than elsewhere, becomes

inflamed and ulcerates; and an intractable and bleeding ulcer is the consequence. Then one of the cysts, more distended than the rest, gives way, discharging its serous contents. Perhaps the opening heals, then again gives way; and this may recur several times, until at last a fungous growth protrudes through the opening. And here the question arises, what is the exact nature of these changes, which, by a slow gradual operation, at last convert a disease so small and simple in its origin, into one so extensive and complicated? This I shall next endeavour to explain; and a series of preparations on the table, with the histories of the cases belonging to them, will enable me to do so.

The first of these is a membranous cyst, which I removed from the breast of a private patient. It is of the size of a large walnut; and you will observe that about one-fourth part of its cavity is occupied by an irregularly shaped excrescence attached to one portion of its internal surface.

Several years ago Mr. Green and myself were present when Mr. Freeman, of Spring Gardens, removed the breast of a female with a similar tumor imbedded in it. The tumor was of about the same size as that which I have just shewn you; and in my notes of the case I find it stated, that "the cyst contained serum, but that about one-third part of its cavity was occupied by an excrescence which came from one part of its inner surface. The excrescence had the appearance of fibrine which had become vascular."

The history of the patient whose case has furnished us with the next preparation, and the accompanying drawing, is highly interesting, and illustrates many circumstances connected with this disease.

This lady consulted me in the month of October 1837, respecting a tumor of the breast, which might be compared as to size to a large nutmeg. It was of a globular shape, and evidently contained fluid. I punctured it with a grooved needle, and a yellow serum escaped. There were no other indications of disease. Afterwards I made a free opening into the cyst with a lancet, and, the whole of the fluid having been evacuated, I introduced a piece of lint, with a view to produce inflammation

and the formation of granulations on its inner surface, which might obliterate its cavity. An abundant suppuration and a good deal of inconvenience followed this trifling operation. At the end of about two months, although the abscess was not properly closed, the patient believing herself to be nearly well, left London of her own accord. I heard nothing of her from this time until, after the lapse of about fifteen months, she again placed herself under my care. In the situation of the cyst which I had laid open there was now a considerable solid tumor, a portion of which, of about half the size of an orange, projected through an opening in the skin, forming an irregularly shaped fungus. There seemed to be no other remedy than that of the removal of the breast by an operation, to which the patient willingly consented; and from which she recovered favourably.

On examining the tumor in its recent state some remains of the original membranous cyst, containing a small quantity of serum, were found at its basis. A large quantity of solid substance projected as an excrescence from the inner surface of the cyst, assuming a peculiar plicated or fimbriated appearance, and a portion of this excrescence protruding through the skin, formed the external fungus. You will see these appearances distinctly visible in the preparation, although not so plainly as before the parts were immersed in alcohol, and they are well represented in this drawing, which is made with Mr. Perry's usual accuracy. The structure of the morbid growth seems to be of the simplest kind. I can compare it to nothing better than fibrine imperfectly organized. (p. 811) Its existence does not seem to be limited to the inside of the cyst, a considerable mass being on the outside, in immediate contact with the gland of the breast. Previously to the operation the remaining part of the breast appeared to be in a healthy condition; but on dissection afterwards I found imbedded in it a great number of membranous cysts, of various sizes, from that of a pea to that of a horsebean. These cysts contained a transparent yellow serum, and were evidently of the same nature with the larger cyst which I had formerly punctured, and in which the fungus had originated afterwards.

The preparation which I now shew you leads me to the history

of a patient who is still under the care of Mr. Keate, in this hospital. Fifteen months ago, being then an out-patient, she had a tumor of the left breast, above the nipple, of the size of a walnut. It was globular and moveable. Mr. Cutler punctured it with a grooved needle, and ascertained that it contained serum. Soon afterwards it was found that a fluid, similar to that which had escaped by the puncture, was discharged by the nipple. From this time the tumor gradually increased to size. Six weeks ago Mr. Keate repeated the puncture with a needle, giving exit to a large quantity of yellow serum. The tumor, in consequence, was much reduced in size, but it soon enlarged again, so as to exceed its former dimensions. On the 21st of last December, Mr. Keate made an incision into it, and the cyst was now so capacious that not less than half a pint of serum was evacuated by the wound. The serum now was tinged with blood, and a good deal of hæmorrhage followed the operation. In the course of a few days a large dark-coloured fungus was seen projecting through the wound. Under these circumstances, on the second of present month, Mr. Keate amputated the breast, and you may here see the morbid appearance which it presents.

The tumor consists of a large membranous cyst, which might have been capable of containing twelve ounces of fluid, if the greater part of its cavity had not been occupied by a great number of excrescences attached to its inner surface. These excrescences vary in size, the smallest being not bigger than a pea, while one of them is of the size of a small orange. They are covered by a thin membrane, which appears to be continuous with, and a reflection of the inner layer of the cyst. When cut into, these excrescences present the appearance of a considerable variety of structure. Some of them may be compared to recently coagulated albumen not yet organized: others, to imperfectly organized fibrine: some of them have an apparent resemblance to fatty tumors, although I do not find that they actually contain any oily matter, and one of them might, on the first view of it, be almost mistaken for medullary disease.

The tumor which is displayed in the next preparation illustrates a still more advanced stage of the disease. I removed it

from the breast of a private patient in the month of November 1836. It had existed for many years gradually, but slowly increasing in size. You perceive that at the time of its removal the tumor was not larger than a small orange, and that it was of an irregular shape. Near the base of the nipple is a membranous cyst, which contained two or three drams of very dark-coloured serum. Some smaller cysts, which also contained serum, are seen in the neighbourhood, and a bristle introduced at one of the ducts of the nipple has entered one of the cysts by a smaller circular aperture. The seat of the tumor, on a superficial view of it, appears to be one uniform mass of solid substance: but on a more close inspection you find it to consist of a congeries of membranous cysts, the cavities of which are completely filled with fibrinous matter. In many of the cysts, on examination with a probe, I found this fibrinous matter to have an attachment to one part of the inner surface, lying in contact with the lining membrane elsewhere, but having no actual adhesion to it.

We can scarcely doubt that if in this case the operation had been deferred until a later period, the growths of fibrinous matter, by which the cysts were occupied, would have contracted universal adhesions to the membrane with which they lay in contact, and that the whole, with the exception of those cysts which still contained serum, would have been identified in one solid mass of substance, in which the original cellular or cystic structure would have entirely disappeared. Of this last change, the preparation which I now shew you, seems to furnish an example. The patient from whom this specimen was taken was under my care in the year 1818. I have no notes of the early history of the case; but the disease had probably been of long duration, as, at the time of my being consulted, the breast had attained an enormous size, being not less than seven pounds in weight. She was a middle-aged person, otherwise in good health, and the skin and the axillary glands were free from disease. Under these circumstances the diseased breast was amputated. The wound healed favourably, and I heard of the patient being alive and well several years afterwards. If you examine the cut (p. 812) surface of the tumor, or rather of that portion of it which is displayed in

the preparation, you will see that the greater part of it is one uniform solid mass, of which it is difficult to describe the structure in words, further than by saying, that in some parts it has an indistinct laminated appearance. There are, however, in one part of it, several membranous cysts of various dimensions, which, when first cut into, were found containing serum. One of those is distinguished from the rest by its greater size, being capable of containing several ounces of fluid, but being also occupied by a large excrescence attached to one part of its inner surface, and projecting into its cavity. This excrescence is of an irregular shape, very similar in appearance to some of those which you have seen in the other preparations. In its recent state it seemed to consist of distinct masses of recently coagulated albumen, semi-pellucid, some of a light yellow, others approaching to a purple colour, and altogether bearing no small resemblance to a bunch of white and purple grapes. These peculiar appearances, of course, have been destroyed by the immersion in alcohol.

Having explained to you these facts in detail, with a view to impress the subject more completely on your minds, I shall endeavour to trace, in a few words, the pathological history which they seem to establish, and which, not only as a matter of science, but in a practical point of view, it is so important for you to understand. It appears, then, to be as follows:—

First: a greater or less number of membranous cysts are generated in the breast, containing serum. The latter is at first of a light yellow colour, and transparent, but afterwards becomes of a darker colour, and opaque. There is reason to believe that these cysts are formed by a dilatation of portions of some of the lactiferous tubes.

Secondly: morbid growths or excrescences are generated from the inner surface of one or more of these cysts, projecting into their cavities. These excrescences seem to consist of albumen or fibrine, which, after some time, (if not immediately) becomes organized. They are covered by a thin delicate membrane, which seems to be reflected over them for the inner surface of the cyst; but whether they are originally formed between two layers of the membrane of the cyst, or whether they are at first

mere deposits of fibrine or albumen on the inner surface of the cyst, a thin membrane being formed on their surface afterwards, remains to be determined by future observations.

Thirdly: there is some reason for believing that a similar growth of fibrinous substance may take place from the external surface of the cysts connecting different cysts with each other; but this point may perhaps require to be illustrated by further investigations.

Fourthly: under certain circumstances the cysts become completely filled up by the morbid growths, so that their cavities are obliterated, the tumor being thus converted into a solid mass, in which, however, the remains of the cysts are perceptible; and this is the prelude to a still further change, in which the greater part of the cysts have wholly disappeared, a solid mass of an indistinctly laminated texture occupying their place.

Fifthly: if one of the membranous cysts be artificially laid open, or if it burst from over-distension with serum, the fibrinous excrescence from its inner surface being no longer restrained by the pressure of the skin, increases in size, and protrudes externally in the form of a fungus, giving to the tumor a new and more formidable character.

In this last stage of the disease, it is evident that spreading ulceration, sloughing, and hæmorrhage, the usual results of an ulcer occurring in a diseased structure, must ensue, and that no remedy is likely to be of any service to the patient, except the removal of the affected parts by a surgical operation.

And this leads us to the concluding and most important part of these inquiries. In considering the treatment of these cases, it is convenient to distinguish those in which the disease is still in its earliest stage, presenting itself in the form of a membranous cyst, or cysts, containing serum, from those in which the growth of a solid fibrinous substance has become superadded to this simple original structure.

In the first order of cases we may venture to evacuate the fluid contents of the cyst by penetrating it with a grooved needle. No inconvenience is ever the result of this trifling operation; and it is often useful by assisting us in our diagnosis, and also by

enabling us to determine whether any growth of solid matter, in connection with the cyst, has yet taken place. But it is not productive of any permanent benefit, as the fluid is always regenerated in the course of two or three days. I have no experience which would lead me to recommend any further or more considerable operation than this. It is needless to remove what appears to be a solitary cyst, as it is always highly probable that there are other cysts in other parts of the breast co-existent with it, which are not yet sufficiently developed to be perceptible through the skin; or otherwise, that such cysts will be formed afterwards if they do not exist already. As to the removal of the entire breast, it is, under these circumstances, an unjustifiable proceeding, unless it be in a (p. 873) few cases in which the cyst or cysts have attained so large a size as to be inconvenient from their bulk. The disease, in its early stage, causes no suffering, and may remain for years, or for the whole of the patient's life, without advancing farther, and, under these circumstances, no harm can possibly arise from delay. Besides: if I am not greatly mistaken, there is a simple and safe mode of treatment which may often be employed with great advantage, and which is not open to those objections to which any severe operation is always liable.

Some years ago, a lady consulted me concerning a small tumor of the breast, near the nipple, and apparently containing fluid. Not at that time knowing any thing better, I recommended that it should be removed by the knife. The day was fixed for the operation, but, in the meantime, some domestic circumstance occurred which made it necessary that it should be postponed. Under these circumstances I proposed to the patient that she should make the experiment of applying a stimulating embrocation to surface of the skin. This accordingly was done, and the result was, that the tumor disappeared. Some time afterwards, another lady consulted me, having a globular tumor of one breast, larger than a pigeon's egg. I punctured it with a grooved needle, and a considerable quantity of serum was drawn off. In a few days, the fluid being re-produced, the tumor, which had wholly disappeared, was as large as ever. I now applied the same treat-

ment as in the former case; and in the course of some weeks the whole of the fluid had become absorbed, and nothing was perceptible, except a slight thickening, apparently formed by the collapsed membrane of the cyst. The thickening disappeared gradually, and when I last saw the patient, three or four years after the time which I have mentioned, there had been no recurrence of the disease. Since these cases occurred, I have had recourse to the same method of treatment in many instances. In some of them the result has been, that the tumor or tumors have entirely disappeared; in others, that without disappearing altogether, they have become very much reduced in size; and it is only in a few instances in which the treatment was not very rigidly pursued, that it has been productive of no manifest advantage.

The application which I have generally made use of on these occasions is the following:—

℞ Spiritus Camphorati, Spiritus tenuioris, aa. ʒiiss; Liqueur plumbi diacetatis, ʒj. fiat Embrocatio.

I have directed the patient to soak a piece of flannel in this embrocation, and to apply it so as to cover that part of the breast in which the tumor is situated, renewing the application six or eight times in the day and night until the skin becomes inflamed; then to omit the application for two or three days, but to resume the use of it as soon as the inflammation has subsided. The period of time during which it is necessary to pursue this method of treatment varies in different cases. In some, all that can be desired is accomplished in the course of three or four weeks; in others, it must be continued, with occasional intermissions, for some months. Other stimulating applications may be occasionally substituted for that which I have just mentioned. Several blisters may be applied in succession; each of them being kept open for a few days with the savine cerate; or a solution of ʒj. of iodine in ʒj. of alcohol may be applied to the skin once or twice daily, by means of a large camel's-hair brush. On the whole, however, I am led to believe, that the embrocation is more efficient than any thing else.

But these remedies are of no avail when the growth of solid substance is begun. In this more advanced period of the disease, no good is to be expected except from the removal of the entire breast; and such an operation may be had recourse to with every prospect of success.

The disease seems to be entirely local. It belongs to the breast, and to nothing else. It does not contaminate either the skin or the lymphatic glands; it is not complicated with any corresponding disease of the viscera; and all the experience which I have had justifies the conclusion, that if care be taken that no portion of the breast is allowed to remain, there is no danger of its recurrence.

A careful observer will find little difficulty in distinguishing cases of this disease from those of the other diseases to which the breast is subject. It is, however, desirable with a view to a more ready and accurate diagnosis, that we should consider what are the diseases with which it is most liable to be confounded. The principal of these are as follows:—

First: a thin membranous cyst, containing a transparent watery fluid, without coagulable matter, is occasionally found in the breast, which may be compared to the membranous cysts, containing pure water, which are sometimes met with in connexion with the liver; and of which I have published some cases in one of the medical journals*; and to the encysted (p. 84) hydrocele of the spermatic cord or testicle. This disease is probably rare, as only two examples of it have fallen under my observation. In one of them the cyst was extracted by an operation; in the other the nature of the fluid having been ascertained by means of a puncture with a grooved needle, the tumor afterwards disappeared under the use of a stimulating embrocation.

Secondly: a cavity is sometimes formed in the breast, containing one or more genuine hydatids. Here there is a single fluctuating tumor, which gradually increases to a large size. If it be freely opened, the hydatids escape, and the cavity in which they were lodged becomes an abscess, which slowly closes and heals.

Thirdly: in a more advanced stage of the disease, it is not un-

* See MEDICAL GAZETTE, vol. i, page 344; and vol. xv, page 25.

frequently mistaken for carcinoma; and I have no doubt that a large proportion of the cases in which it has been supposed that an operation has effected a permanent cure of the last-mentioned disease, have been in reality of this description.

I have hitherto confined myself to the description of the origin, progress, and treatment, of this disease of the breast, without venturing to give it a name.

It is, however, necessary that we should have the means of distinguishing it in conversation and in writing; and I would suggest "the sero-cystic tumor of the breast" as being an appropriate appellation—preferable, at all events, to a mere arbitrary term; inasmuch as it expresses with sufficient precision the character which the tumor possesses in its origin.

THE END

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JAMES PARKINSON

From the Jubilee Book of the British Dental Association. London, John Bale,
Sons & Danielsson, 1930. p. 8

MEDICAL CLASSICS

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James Parkinson

BIOGRAPHY

- 1755 April 11, born, and on April 29, baptized and registered in St. Leonard's Shoreditch Parish Register, Middlesex. Son of Jno. Parkinson, surgeon, who died in 1784. Lived at No. 1 Hoxton Square, London.
- 1781 Age 26. Married Mary Dale in St. Leonard's Shoreditch Church on May 21. Had three sons, one a doctor, and two daughters.
- 1785 Age 30. In active practice and attended Hunter's course of lectures on surgery.
- 1794 Age 39. Examined on oath before the privy council in connection with the so-called "Pop-gun Plot" to assassinate George III. He admitted being a member of the Committee of Correspondence of the London Corresponding Society and of the Constitutional Society.
- 1807 Age 52. Original member of the Geological Society on its foundation.
- 1817 Age 62. Wrote An Essay on the Shaking Palsy.
- 1824 Age 69. Died Dec. 21, in Kingsland Road, only a short distance from where he had always lived. Buried in Hoxton Parish burying ground, the church yard of St. Leonard's Shoreditch church. No stone can now be found.

Also:

Fellow of Royal College of Surgeons.

Member of the Wernerian Society of Edinburgh.

Member of the Caesarean Society of Moscow.

He was a man of the Old Master type described by Holmes, rather than the highly specialized scarabaeist. Master of medicine, chemistry, geology, paleontology and oryctology, he was a writer of many textbooks, great as a compiler, keen in observation and desirous of seeing everything named and placed in its proper class. (Rowntree).

EPONYMS

DISEASE OR SYNDROME: Paralysis agitans or shaking palsy: a disease of late life, progressive in its course, and marked by a characteristic tremor of the muscles, weakness, delay of voluntary motion, a peculiar festinating gait, and muscular contraction, causing peculiar and characteristic positions of the limbs and head. The disease is attended with excessive sweating and feelings of heat and cold. (Dorland)

FACIES OR SIGN: A stolid expression of the face, characteristic of paralysis agitans.

BIBLIOGRAPHY OF WRITINGS

A—Army Medical Library.

B—New York State Library.

C—New York Academy of Medicine Library.

1. Observations on Dr. Hugh Smith's Philosophy of physic. Anonymous but ascribed to James Parkinson, 1780.
2. Revolution without bloodshed; or reformation preferable to revolt. Pamphlet, 1794.
3. A vindication of the London Corresponding Society. Pamphlet, 1794.
4. Assassination of the King. A letter to Mr. John Smith, 1795.
5. The chemical pocket-book; or memoranda chemica; arranged in a compendium of chemistry. 1799. 1. ed., 12°. (Same) 1799. 1. Amer. ed. (Same) 1801. 2. ed. (Same) Philadelphia, Humphrey, 1802. xii, 215 pp., 2 pl. from the London 2 ed. of 1801. In A and C. (Same) 1803. 3. ed. (Same) 1809. 4. ed.

6. Medical admonitions to families respecting the preservation of health and the treatment of the sick. Also, a tablet of symptoms, serving to point out the degree of danger, and to distinguish one disease from another; with observations on the improper indulgence of children. 1799. 1. ed., 12°. (Same) London, Whittingham, 1801. 4. ed., 12°, 35 1., 548 pp. In C. (Same) Portsmouth, N. H., Pierce, 1802. 1. Amer. from 4. London ed., 8°, 520 pp. In A, B and C. (Same) London, Symonds, 1807. 5 ed., 8°, xx, 503 pp. In A.
7. Dangerous sports; a tale addressed to children. 1800. 1. ed., 16°. (Same) 1808. 2. ed.
8. The hospital pupil; or, observations addressed to the parents of youths intended for the profession of medicine and surgery; on their previous education, pecuniary resources, and on the order of their professional studies, with hints to the young pupil on the prosecution of hospital studies, on entering into practice, and on medical jurisprudence. London, Symonds, 1800. 16°, 159 pp. In C. (Same) London, Sherwood, 1817. 2. ed., 12°, 208 pp. In A.
9. The villager's friend and physician; or a familiar address on the preservation of health, and the removal of disease on its first appearance; supposed to be delivered by a village apothecary, with cursory observations on the treatment of children, on sobriety, industry, etc. London, Sammells, 1800. 12°, 85 pp. In C. (Same) London, Whittingham, 1804. 2. ed., 12°, 71 pp., 1 pl. In A.
10. Hints for the improvement of trusses; intended to render their use less inconvenient, and to prevent the necessity of an understrap. With the description of a truss of easy construction and slight expense, for the use of the laboring poor. London, Symonds, 1802. 8°, viii, 9-22 pp., 1 pl. In A.
11. The way to health. 1802. 8°.
12. Organic remains of a former world; an examination of the mineralized remains of the vegetables and animals of the antediluvian world; generally termed extravenous fossils. Vol. 1, 1804; 2, 1808; 3, 1811.

13. Observations on the nature and cure of gout; on nodes of the joints; and on the influence of certain articles of diet, in gout, rheumatism and gravel. London, Symonds, 1805. 8°, viii, 174 pp. In A and C.
14. Remarks on Mr. Whitebread's plan for the education of the poor. 1807. 8°.
15. Observations on the excessive indulgence of children. 1807. 8°.
16. Mad-houses. Observations on the act regulating mad-houses, and a correction of the statements in the case of Benjamin Elliott, convicted of illegally confining Mary Daintree; with remarks addressed to the friends of insane persons. London, Whittingham and Rowland, 1811. 8°, vii, 48 pp. In A and B. Also, rev.: Edinb. Med. Jour., 7: 371-377, 1811.
17. A case of trismus, successfully treated. By John Parkinson, communicated by James Parkinson. Read June 18, 1811. Med.-Chir. Trans., 2: 291-295, 1811.
18. Case of diseased appendix vermiformis. By John Parkinson, communicated by James Parkinson. Read Jan. 21, 1812. Ibid., 3: 57-58, 1812. Also: reference, 4 lines, Edinb. Med. Jour., 9: 198, 1813.
19. An essay on the shaking palsy. London, Whittingham and Rowland, 1817. 12°, iv, 66 pp. In A and C. (Same) Facsimile ed., Amer. Med. Assn. Press, Chicago, 1917. Also: Arch. Neur. and Psych., 7: 681-710, 1922..
20. Outlines of Oryctology. 1822. 340 pp. Passed through 3 editions.
21. John Hunterian Reminiscences—transcribed by James Parkinson. Edited by his son, J. W. K. Parkinson. London, 1833. 4°. In A.
22. Also author of several geological papers in Nicholson's "Journal", 1809-1812, and in the first, second and fifth volumes of the Geological Society's Transactions, 1811-1818.

BIOGRAPHIES

- Biography by G. S. Boulger. Dict. Nat. Biog., 43: 314, 1895.
 Biography by L. G. Rowntree. Johns Hopk. Hosp. Bull., 23:
 33-45, 1912.
 James Parkinson and his essay on paralysis agitans. By R. T.
 Williamson. Janus, Leyde, 29: 193-197, 1925.
 Note on history of appendicitis in children. By J. Ruhräh.
 Amer. Jour. Dis. Child., 49: 474-476, 1935.

INDEX TO BIBLIOGRAPHY

	Reference	Year
Appendix vermiciformis.....	18	1812
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Chemical pocket-book.....	5	1799
Children, indulgence of.....	15	1807
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Villager's friend.....	9	1800
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INTRODUCTION

James Parkinson had written on several medical subjects before he published *An essay on the shaking palsy* in 1817. He had reported in 1812 the first case of appendicitis in English, this case being also the first in which perforation was recognized as the cause of death. (H. A. Kelly.) He had published several books of medical advice for the layman, *Medical admonitions to families . . .*, *Dangerous sports . . .*, *The hospital pupil; or, observations addressed to the parents of youths intended for the profession of medicine and surgery . . .*, and *The villager's friend and physician . . .*. But James Parkinson is remembered today because of the condition which is now known by his name, Parkinson's disease or shaking palsy.

Parkinson himself tells us in the *Essay* that different forms of tremors had been noted by Galen, Sylvius de la Boë, Juncker, Cullen and Sauvages. The author quotes freely in Latin from these earlier writers and points out differences in their descriptions and conceptions of types of tremors. He thus shows that he was acquainted with medical literature and had a good education.

Why has this *Essay* covering only 66 small pages brought fame to its writer? The answer is found in the clear, exact, and complete picture of the disease syndrome which Parkinson gives us. The reader can see vividly the patients described, their characteristic tremor, posture and gait. The course of the disease is dramatic in its description. Several case records follow. The author then discusses varieties of tremor, palpitations and convulsions, and explains how the disease differs from others with which it is most easily confused. Parkinson attempts to give some etiologic factors such as trauma and disease of the medulla spinalis but he regrets that lack of autopsy study prevents him from knowing the pathologic changes in the brain. Therefore he knows little of the etiology or true nature of the condition. Finally the treatments recommended are interesting from an historical viewpoint, i.e., bleeding, blisters, vesicatories and making an issue with caustic. At no point does Parkinson describe the characteristic facies or "mask" which has become associated with his name.

Because of the interest which Parkinson aroused in the shaking palsy (he tells us this was the chief aim in writing the *Essay*), considerable advance has been made in the knowledge of the pathologic processes. It is now recognized that there is a degeneration of the globus pallidus and ansa lenticularis with disappearance of ganglion cells and fibers, increase of glia fibers, softening and lacunar formations (Wechsler). Other pathologic changes have been found in other parts of the brain and the subject is still controversial. (Jour. Amer. Med. Assn., 100:1602-1603, 1933.)

Recently much interest has grown up around the so-called parkinsonian syndrome, it being recognized that many of the signs described by Parkinson follow encephalitis. These cases, of course, come on acutely, usually in young people and reveal signs of inflammation, frequently in the substantia nigra and midbrain structure. Acute cases also may follow hemorrhage into the basal ganglion or syphilis in this region. Chronic cases of the syndrome occur with neoplasms or arteriosclerosis. Relation of trauma to the syndrome was studied in 1932 by Naville and de Morsier and by Minovici, Paulian and Stanesco; they all conclude that in some cases trauma may be an indirect etiologic factor.

Parkinson wrote a valuable article in 1817; 121 years later we know a little more of the condition but there is much more to be learned. Only careful study and research will bring forth the ultimate answer to the problems still present.



An Essay on the Shaking Palsy

BY

JAMES PARKINSON

Member of the Royal College of Surgeons

London: Printed by Whittingham and Rowland, Goswell Street,
for Sherwood, Neely, and Jones, Paternoster Row, 1817

PREFACE

THE advantages which have been derived from the caution with which hypothetical statements are admitted, are in no instance more obvious than in those sciences which more particularly belong to the healing art. It therefore is necessary, that some conciliatory explanation should be offered for the present publication: in which, it is acknowledged, that mere conjecture takes the place of experiment; and, that analogy is the substitute for anatomical examination, the only sure foundation for pathological knowledge.

When, however, the nature of the subject, and the circumstances under which it has been here taken up, are considered, it is (p. ii) hoped that the offering of the following pages to the attention of the medical public, will not be severely censured. The disease, respecting which the present inquiry is made, is of a nature highly afflictive. Notwithstanding which, it has not yet obtained a place in the classification of nosologists; some have regarded its characteristic symptoms as distinct and different diseases, and others have given its name to disease differing es-

entially from it; whilst the unhappy sufferer has considered it as an evil, from the domination of which he had no prospect of escape.

The disease is of long duration: to connect, therefore, the symptoms which occur in its later stages with those which mark its commencement, requires a continuance of observation of the same case, or at least a correct history of its symptoms, even for several years. Of both these advantages the writer has had the opportunities of availing (p. iii) himself; and has hence been led particularly to observe several other cases in which the disease existed in different stages of its progress. By these repeated observations, he hoped that he had been led to a probable conjecture as to the nature of the malady, and that analogy had suggested such means as might be productive of relief, and perhaps even of cure, if employed before the disease had been too long established. He therefore considered it to be a duty to submit his opinions to the examination of others, even in their present state of immaturity and imperfection.

To delay their publication did not, indeed, appear to be warrantable. The disease had escaped particular notice; and the task of ascertaining its nature and cause by anatomical investigation, did not seem likely to be taken up by those who, from their abilities and opportunities, were most likely to accomplish it. That these friends to humanity (p. iv) and medical science, who have already unveiled to us many of the morbid processes by which health and life is abridged, might be excited to extend their researches to this malady, was much desired; and it was hoped, that this might be procured by the publication of these remarks.

Should the necessary information be thus obtained, the writer will repine at no censure which the precipitate publication of mere conjectural suggestions may incur; but shall think himself fully rewarded by having excited the attention of those, who may point out the most appropriate means of relieving a tedious and most distressing malady.

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CHAPTER I. DEFINITION—HISTORY—ILLUSTRATIVE CASES
SHAKING PALSY (PARALYSIS AGITANS)

(Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured)

The term Shaking Palsy has been vaguely employed by medical writers in general. By some it has been used to designate ordinary (p. 2) cases of Palsy, in which some slight tremblings have occurred; whilst by others it has been applied to certain anomalous affections, not belonging to Palsy.

The shaking of the limbs belonging to this disease was particularly noticed, as will be seen when treating of the symptoms, by Galen, who marked its peculiar character by an appropriate term. The same symptom, it will also be seen, was accurately treated of by Sylvius de la Boë. Juncker also seems to have referred to this symptom: having divided tremor into active and passive, he says of the latter, "*ad affectus semiparalyticos pertinent; de qualibus hic agimus, quique tremores paralytoidei vocantur.*" Tremor has been adopted, as a genus, by almost every nosologist; but always unmarked, in their several definitions, by such char-

acters as would embrace this disease. The celebrated Cullen, with his accustomed accuracy observes, "*Tremorem, utpote semper symptomaticum, in numerum generum recipere nollem; species autem a Sauvagesio recensitas, prout mihi vel astheniae vel paralysios, vel convulsionis symptomata esse videntur, (p. 3) his subjungam**. Tremor can indeed only be considered as a symptom, although several species of it must be admitted. In the present instance, the agitation produced by the peculiar species of tremor, which here occurs, is chosen to furnish the epithet by which this species of Palsy, may be distinguished.

HISTORY

So slight and nearly imperceptible are the first inroads of this malady, and so extremely slow is its progress, that it rarely happens, that the patient can form any recollection of the precise period of its commencement. The first symptoms perceived are, a slight sense of weakness, with a proneness to trembling in some particular part; sometimes in the head, but most commonly in one of the hands and arms. These symptoms gradually increase in the part first affected; and at an uncertain period, but seldom in less than twelve months or more, the morbid influence is felt in some other part. Thus assuming one of the (p. 4) hands and arms to be first attacked, the other, at this period becomes similarly affected. After a few more months the patient is found to be less strict than usual in preserving an upright posture: this being most observable whilst walking, but sometimes whilst sitting or standing. Sometime after the appearance of this symptom, and during its slow increase, one of the legs is discovered slightly to tremble, and is also found to suffer fatigue sooner than the leg of the other side: and in a few months this limb becomes agitated by similar tremblings, and suffers a similar loss of power.

Hitherto the patient will have experienced but little inconvenience; and befriended by the strong influence of habitual endurance, would perhaps seldom think of his being the subject of disease, except when reminded of it by the unsteadiness of his hand, whilst writing or employing himself in any nicer kind of

* *Synopsis Nosologiae Methodicae*.—Tom. ii. p. 195.

manipulation. But as the disease proceeds, similar employments are accomplished with considerable difficulty, the hand failing to answer with exactness to the dictates of the will. Walking (p. 5) becomes a task which cannot be performed without considerable attention. The legs are not raised to that height, or with that promptitude which the will directs, so that the utmost care is necessary to prevent frequent falls.

At this period the patient experiences much inconvenience, which unhappily is found daily to increase. The submission of the limbs to the directions of the will can hardly ever be obtained in the performance of the most ordinary offices of life. The fingers cannot be disposed of in the proposed directions, and applied with certainty to any proposed point. As time and the disease proceed, difficulties increase: writing can now be hardly at all accomplished; and reading, from the tremulous motion, is accomplished with some difficulty. Whilst at meals the fork not being duly directed frequently fails to raise the morsel from the plate: which, when seized, is with much difficulty conveyed to the mouth. At this period the patient seldom experiences a suspension of the agitation of his limbs. Commencing, for instance in one arm, the (p. 6) wearisome agitation is borne until beyond sufferance, when by suddenly changing the posture it is for a time stopped in that limb, to commence, generally, in less than a minute in one of the legs, or in the arm of the other side. Harassed by this tormenting round, the patient has recourse to walking, a mode of exercise to which the sufferers from this malady are in general partial; owing to their attention being thereby somewhat diverted from their unpleasant feelings, by the care and exertion required to ensure its safe performance.

But as the malady proceeds, even this temporary mitigation of suffering from the agitation of the limbs is denied. The propensity to lean forward becomes invincible, and the patient is thereby forced to step on the toes and fore part of the feet, whilst the upper part of the body is thrown so far forward as to render it difficult to avoid falling on the face. In some cases, when this state of the malady is attained, the patient can no longer exercise himself by walking in his usual manner, but is thrown on the

toes and forepart of the feet; being, at the same (p. 7) time, irresistibly impelled to take much quicker and shorter steps, and thereby to adopt unwillingly a running pace. In some cases it is found necessary entirely to substitute running for walking; since otherwise the patient, on proceeding only a very few paces, would inevitably fall.

In this stage, the sleep becomes much disturbed. The tremulous motion of the limbs occur during sleep, and augment until they awaken the patient, and frequently with much agitation and alarm. The power of conveying the food to the mouth is at length so much impeded that he is obliged to consent to be fed by others. The bowels, which had been all along torpid, now, in most cases, demand stimulating medicines of very considerable power: the expulsion of the faeces from the rectum sometimes requiring mechanical aid. As the disease proceeds towards its last stage, the trunk is almost permanently bowed, the muscular power is more decidedly diminished, and the tremulous agitation becomes violent. The patient walks now with great difficulty, and unable any longer to support himself (p. 8) with his stick, he dares not venture on this exercise, unless assisted by an attendant, who walking backwards before him, prevents his falling forwards, by the pressure of his hands against the fore part of his shoulders. His words are now scarcely intelligible; and he is not only no longer able to feed himself, but when the food is conveyed to the mouth, so much are the actions of the muscles of the tongue, pharynx, &c. impeded by impaired action and perpetual agitation, that the food is with difficulty retained in the mouth until masticated; and then as difficultly swallowed. Now also, from the same cause, another very unpleasant circumstance occurs: the saliva fails of being directed to the back part of the fauces, and hence is continually draining from the mouth, mixed with the particles of food, which he is no longer able to clear from the inside of the mouth.

As the debility increases and the influence of the will over the muscles fades away, the tremulous agitation becomes more vehement. It now seldom leaves him for a moment; but even when exhausted (p. 9) nature seizes a small portion of sleep, the motion

becomes so violent as not only to shake the bed-hangings, but even the floor and sashes of the room. The chin is now almost immovably bent down upon the sternum. The slops with which he is attempted to be fed, with the saliva, are continually trickling from the mouth. The power of articulation is lost. The urine and faeces are passed involuntarily; and at the last, constant sleepiness, with slight delirium, and other marks of extreme exhaustion, announce the wished-for release.

CASE I

Almost every circumstance noted in the preceding description, was observed in a case which occurred several years back, and which, from the particular symptoms which manifested themselves in its progress; from the little knowledge of its nature, acknowledged to be possessed by the physician who attended; and from the mode of its termination; excited an eager wish to acquire some further knowledge of its nature and cause.

(p. 10) The subject of this case was a man rather more than fifty years of age, who had industriously followed the business of a gardener, leading a life of remarkable temperance and sobriety. The commencement of the malady was first manifested by a slight trembling of the left hand and arm, a circumstance which he was disposed to attribute to his having been engaged for several days in a kind of employment requiring considerable exertion of that limb. Although repeatedly questioned, he could recollect no other circumstance which he could consider as having been likely to have occasioned his malady. He had not suffered much from Rheumatism, or been subject to pains of the head, or had ever experienced any sudden seizure which could be referred to apoplexy or hemiplegia. In this case, every circumstance occurred which has been mentioned in the preceding history.

CASE II

The subject of the case which was next noticed was casually met with in the street. It was a man sixty-two years of age; the (p. 11) greater part of whose life had been spent as an attendant at a magistrate's office. He had suffered from the dis-

ease about eight or ten years. All the extremities were considerably agitated, the speech was very much interrupted, and the body much bowed and shaken. He walked almost entirely on the fore part of his feet, and would have fallen every step if he had not been supported by his stick. He described the disease as having come on very gradually, and as being, according to his full assurance, the consequence of considerable irregularities in his mode of living, and particularly of indulgence in spirituous liquors. He was the inmate of a poor-house of a distant parish, and being fully assured of the incurable nature of his complaint, declined making any attempts for relief.

CASE III

The next case was also noticed casually in the street. The subject of it was a man of about sixty-five years of age, of a remarkable athletic frame. The agitation of the limbs, and indeed of the head and of the whole body, was too vehement to allow it (p. 12) to be designated as trembling. He was entirely unable to walk; the body being so bowed, and the head thrown so forward, as to oblige him to go on a continued run, and to employ his stick every five or six steps to force him more into the upright posture, by projecting the point of it with great force against the pavement. He stated, that he had been a sailor, and attributed his complaints to having been for several months confined in a Spanish prison, where he had, during the whole period of his confinement, lain upon the bare damp earth. The disease had here continued so long, and made such a progress, as to afford little or no prospect of relief. He besides was a poor mendicant, requiring as well as the means of medical experiment, those collateral aids which he could only obtain in a hospital. He was therefore recommended to make trial if any relief could, in that mode, be yielded him. The poor man, however, appeared to be by no means disposed to make the experiment.

(p. 13) CASE IV

The next case which presented itself was that of a gentleman about fifty-five years, who had first experienced the trembling of the arms about five years before. His application was on ac-

count of a considerable degree of inflammation over the lower ribs on the left side, which terminated in the formation of matter beneath the fascia. About a pint was removed on making the necessary opening; and a considerable quantity discharged daily for two or three weeks. On his recovery from this, no change appeared to have taken place in his original complaint; and the opportunity of learning its future progress was lost by his removal to a distant part of the country.

CASE V

In another case, the particulars of which could not be obtained, and the gentleman, the lamented subject of which was only seen at a distance, one of the characteristic symptoms of this malady, the inability for motion, except in a running pace, appeared to exist in an extraordinary degree. It seemed (p. 14) to be necessary that the gentleman should be supported by his attendant, standing before him with a hand placed on each shoulder, until, by gently swaying backward and forward, he had placed himself in equipoise; when, giving the word, he would start in a running pace, the attendant sliding from before him and running forward, being ready to receive him and prevent his falling, after his having run about twenty paces.

CASE VI

In a case which presented itself to observation since those above-mentioned, every information as to the progress of the malady was very readily obtained. The gentleman who was the subject of it is seventy-two years of age. He has led a life of temperance, and has never been exposed to any particular situation or circumstance which he can conceive likely to have occasioned, or disposed to this complaint; which he rather seems to regard as incidental upon his advanced age, than as an object of medical attention. He however recollects, that about twenty years ago, he was troubled (p. 15) with lumbago, which was severe and lasted some time. About eleven or twelve, or perhaps more, years ago, he first perceived weakness in the left hand and arm, and soon after found the trembling had commenced. In

about three years afterwards the right arm became affected in a similar manner: and soon afterwards the convulsive motions affected the whole body, and began to interrupt the speech. In about three years from that time the legs became affected. Of late years the action of the bowels had been very much retarded; and at two or three different periods had, with great difficulty, been made to yield to the action of very strong cathartics. But within the last twelve months this difficulty has not been so great; perhaps owing to an increased secretion of mucus, which envelopes the passing faeces, and which precedes and follows their discharge in considerable quantity.

About a year since, on waking in the night, he found that he had nearly lost the use of the right side, and that the face was much drawn to the left side. His medical (p.16) attendant saw him the following day, when he found him languid, with a small and quick pulse, and without pain in the head or disposition to sleep. Nothing more therefore was done than to promote the action of the bowels, and apply a blister to the back of the neck, and in about a fortnight the limbs had entirely recovered from their palsied state. During the time of their having remained in this state, neither the arm nor the leg of the paralytic side was in the least affected with the tremulous agitation; but as their paralysed state was removed, the shaking returned.

At present he is almost constantly troubled with the agitation, which he describes as generally commencing in a slight degree, and gradually increasing, until it arises to such a height as to shake the room; when, by a sudden and somewhat violent change of posture, he is almost always able to stop it. But very soon afterwards it will commence in some other limb, in a small degree, and gradually increase in violence, but he does not remember the thus checking of it, to have been followed by any injurious (p. 17) effect. When the agitation had not been thus interrupted, he stated, that it gradually extended through all the limbs, and at last affected the whole trunk. To illustrate his observation as to the power of suspending the motion by a sudden change of posture, he, being then just come in from a walk, with every limb shaking, threw himself rather violently into a

chair, and said, "Now I am as well as ever I was in my life." The shaking completely stopped; but returned within two minutes' time.

He now possessed but little power in giving a required direction to the motions of any part. He was scarcely able to feed himself. He had written hardly intelligibly for the last three years; and at present could not write at all. His attendants observed, that of late the trembling would sometimes begin in his sleep, and increase until it awakened him: when he always was in a state of agitation and alarm.

On being asked if he walked under much apprehension of falling forwards? he said he suffered much from it; and replied in the (p. 18) affirmative to the question, whether he experienced any difficulty in restraining himself from getting into a running pace? It being asked, if whilst walking he felt much apprehension from the difficulty of raising his feet, if he saw a rising pebble in his path? he avowed, in a strong manner, his alarm on such occasion; and it was observed by his wife, that she believed, that in walking across the room he would consider as a difficulty the having to step over a pin.

The preceding cases appear to belong to the same species: differing from each other, perhaps, only in the length of time which the disease had existed, and the stage at which it had arrived.

(p. 19) CHAP. II. PATHOGNOMONIC SYMPTOMS EXAMINED—
TREMOR COACTUS—SCELOTYRBE FESTINANS

It has been seen in the preceding history of the disease, and in the accompanying cases, that certain affections, the tremulous agitation, and the almost invincible propensity to run, when wishing only to walk, each of which has been considered by nosologists as distinct diseases, appear to be pathognomonic symptoms of this malady. To determine in which of these points of view these affections ought to be regarded, an examination into their nature, and an inquiry into the opinions of preceding writers respecting them, seem necessary to be attempted.

I. Involuntary tremulous motion, with lessened voluntary muscular power, in parts, not in action, and even supported

It is necessary that the peculiar nature of this tremulous motion should be ascertained, as well for the sake of giving to it its proper (p. 20) designation, as for assisting in forming probable conjectures, as to the nature of the malady, which it helps to characterise. Tremors were distinguished by Juncker into Active, those proceeding from sudden affection of the minds, as terror, anger, &c. and Passive, dependant on debilitating causes, such as advanced age, palsy, &c.*. But a much more satisfactory and useful distinction is made by Sylvius de la Boë into those tremors which are produced by attempts at voluntary motion, and those which occur whilst the body is at rest†. Sauvages distinguishes the latter of these species (*Tremor* (p. 21) *Coactus*) by observing, that the tremulous parts leap, and as it were vibrate, even when supported: whilst every other tremor, he observes, ceases, when the voluntary exertion for moving the limb stops, or the part is supported, but returns when we will the limb to move; whence, he says, tremor is distinguished from every other kind of spasm‡.

A small degree of attention will be sufficient to perceive, that Sauvages, by this just distinction, actually separates this kind of tremulous motion, and which is the kind peculiar to this dis-

* Junckeri conspect, de tremore.

† Sect. V. Ubi autem solito pauciores deferunter ad eadem organa spiritus animales, imperfectae ac imbecillae observantur fieri eadem functiones, in motu tremulo et infirmo, nec diu durante, in visu debili, ac mox defatigato, &c.

Sect. XIX. Inaequaliter, inordinate, ac praeter contraque voluntatem moventur spiritus animales per nervos ad partes mobiles, in motu convulsivo, ac tremore, quassuve membrorum coacto.

Distinguendus namque his tremor quiescente licet ac decumbente corpore molustus a motu tremulo, de quo dictum. Sect. V. Quique quiescente corpore cessat, eodemque iterum moto repetit.

Sect. XXV. Coactus tremor debetur animalibus spiritibus inordinate ac continuo, cum aliquo impetu ad trementium membrorum musculos per nervos propulsis: sive fuerit is universalis, sive particularis, sive corpus fuerit ad huc robustum sive debile, Sylvii de la Boë. Prax. lib. i. cap. xlii.

‡ Nosolog. Methodic. Auctore Fr. Boissier de Sauvages, Tomi. II. Partis ii. p. 54. 1763.

ease, from the Genus Tremor. In doing this he is fully warranted by the observations of Galen on the same subject, as noticed by Van Swieten*. "Binas has tremoris species† Galenus subtiliter (p. 22) distinxit, atque etiam diversis nominibus insignivit, tremor enim (τρόμος) facultatis corpus moventis et vehentis infirmitate oboritur. Quippe nemo, qui artus movere non instituerit tremet. Palpitantes autem partes, etiam in quiete fuerint, etiamsi nullum illis motum induxeris palpitant. Ideo primam (*posteriolem*) modo descriptam tremoris speciem, quando quiescenti homini involuntariis illis et alternis motibus agitantur membra, palpitationem (πάλμον) dixit, posteriorem (*primam*) vero, quae non fit nisi homo conetur partes quasdam movere tremorem vocavit."

Under this authority the term palpitation may be employed to mark those morbid motions which chiefly characterise this disease, notwithstanding that this term has been anticipated by Sauvages, as characteristic of another species of tremor‡. The (p. 23) separation of palpitation of the limbs (*Palmos* of Galen, *Tremor Coactus* of de la Boë) from tremor, is the more necessary to be insisted on, since the distinction may assist in leading to a knowledge of the seat of the disease. It is also necessary to bear in mind, that this affection is distinguishable from tremor, by the agitation, in the former, occurring whilst the affected part is supported and unemployed, and being even checked by the adoption of voluntary motion: whilst in the latter, the tremor is induced immediately on bringing the parts into action. Thus

* Comment. in Herman. Boerhaav. Aphorismos. Tom. ii. p. 181.

† De tremore. Cap. 3 and 4. Chart, Tom. vii. p. 200, 201.

‡ Sect. XVI. *Tremor palpitans*, Preysinger classis morborum. *Palmos* Galeni.

In tremoribus vulgaribus, aequalibus temporum intervallis, non musculus, sed artus ipsemet alternation attollitur aut deprimitur, aut in oppositas partes it atque redit per minima tamen spatiola; in palpitatione vero sine ullo ordine musculi unius lacertus subito subsilit, nec regulariter continuoque movetur, sed nunc semel aut bis, nunc minime intra idem tempus subsilit; an causa irritans in sensorio communi, an in musculo ipse palpitante Quaerenda sit, ignoramus. *Nosologiae Methodicae*, Vol. I. p. 559 1768.

But the adoption which Sauvages has made of this term, will not be regarded as an absolute prohibition from the employment of it here; since the tremor palpitans of Sauvages should be considered rather as a palpitation of the muscles, whilst the motion which is so prominent a symptom in this disease, may be considered as a palpitation of the limbs.

an artist, afflicted with the malady here treated of, whilst his hand and arm is palpitating strongly, will seize his pencil, and the motions will be suspended, allowing (p. 24) him to use it for a short period; but in tremor, if the hand be quite free from the affection, should the pen or pencil be taken up, the trembling immediately commences.

II. A propensity to bend the trunk forwards, and to pass from a walking to a running pace

This affection, which observation seems to authorise the being considered as a symptom peculiar to this disease, has been mentioned by few nosologists: it appears to have been first noticed by Gaubius, who says, "Cases occur in which the muscles duly excited into the action by the impulse of the will, do then, with an unbidden agility, and with an impetus not to be repressed, accelerate their motion, and run before the unwilling mind. It is a frequent fault of the muscles belonging to speech, nor yet of these alone: I have seen one, who was able to run, but not to walk*."

(p. 25) Sauvages, referring to this symptom, says, another disease which has been very rarely seen by authors, appears to be referable to the same genus (*Scelotyrbe*, of which he makes *Chorea sancti viti* the first species); which, he says, "I think cannot be more fitly named than hastening or hurrying *Scelotyrbe* (*Scelotyrbem festinantem, seu festiniam*)."

Scelotyrbe festinans, he says, is a peculiar species of *scelotyrbe*, in which the patients, whilst wishing to walk in the ordinary mode, are forced to run, which has been seen by Carguet and by the illustrious Gaubius; a similar affection of the speech, when the tongue thus outruns the mind, is termed volubility. Mons. de Sauvages attributes this complaint to a want of flexibility in the muscular fibres. Hence, he supposes, that the patients make

* Est et ubi muscoli, recte quidem ad voluntatis nutum in actum concitati, injussa dein agilitate atque impetu non reprimendo motus suos accelerant, mentemque invitam praecurrunt. Vitium loquelae musculis frequens, nec his solis tamen proprium: vidid enim, qui currere, non gradi, poterat*.

Institution, Patholog. Medicinal. Auctore. H. D. Gaubio. 751.

shorter steps, and strive with a more than common exertion or impetus to overcome the resistance; walking with a quick and hastened step, as if hurried along against their will. *Chorea Viti*, he (p. 26) says. attacks the youth of both sexes, but this disease only those advanced in years; and adds, that it has hitherto happened to him to have seen only two of these cases; and that he has nothing to offer respecting them, either in theory or practice*.

(p. 27) Having made the necessary inquiries respecting these two affections, *Tremor coactum* of Sylvius de la Boë and of Sauvages, and *Scelotyrbe festinans* of the latter nosologist, which appear to be characteristic symptoms of this disease, it becomes necessary, in the next place, to endeavour to distinguish this disease from others which may bear a resemblance to it in some particular respects.

CHAP. III. SHAKING PALSY DISTINGUISHED FROM OTHER DISEASES WITH WHICH IT MAY BE CONFOUNDED

Treating of a disease resulting from an assemblage of symptoms, some of which do not appear to have yet engaged the general notice of the profession, particular care is required whilst endeavouring to mark its diagnostic characters. It is sufficient,

* Ad idem genus morbi altera species rarissima ab auctoribus praeterivisa referenda videtur, quam non aptius nominari posse putem quam scelotyrbem festinantem, seu festiniam.

Sect. II. *Scelotyrbe festinans*; est peculiaris scelotyrbes species in qua aegri solito more dum gradi volunt currere coguntur, quod videre est apud D. Carquet, et observavit Leydae illustr. Gaubius. *Patholog. instit.* 751, et in loquela haec *volubilitas* dicitur qua lingua praecurrit mentum. Video actu mulierem sexagenariam hoc affectam morbo siccitati nervorum tribuendo; laborat enim rheumatismo sicco, seu ab acrimonia sanguinis, dolores nocte a calore recrudescunt, a thermis non sublevantur; ei praescripsi phebotoMIAM, et praemissis jusculis ex lactuca, endivia, et collo arietis, lene catharticum, inde vero lacticia.

Est affinitas cum scelotyrbe, chorea viti, deest flexibilitas in fibris musculorum; unde motus breves edunt, et conatu seu impetu solito majori, cum resistentiam illam superare nituntur, velut inviti festinant, ac praecipiti seu concitato passu gradiuntur. Chorea viti pueros, puellasve impuberes aggreditur; festinia vero senes, et duos tantum hactenus observare mihi contigit. Quam multos autem videmus morbos, paucissimosque observamus. De theoria et praxi nihil habeo quod dicam; etenim sola experientia praxim cuiusvis morbi determinat, et ex hac pro felici vel infausto successu theoria dein elicienda est. *Nosolog. Methodic.* Auctore, Fr. Boissier de Sauvages. Tomi. ii. Part ii. p. 108.

in general, to point out the characteristic differences which are observable between diseases in some respects resembling each other. But in this case more is required: it is necessary to show that it is a disease (p. 28) which does not accord with any which are marked in the systematic arrangements of nosologists; and that the name by which it is here distinguished has been hitherto vaguely applied to diseases very different from each other, as well as from that to which it is now appropriated.

Palsy, either consequent to compression of the brain, or dependent on partial exhaustion of the energy of that organ, may, when the palsied limbs become affected with tremulous motions, be confounded with this disease. In those cases the abolition or diminution of voluntary muscular action takes place suddenly, the sense of feeling being sometimes also impaired. But in this disease, the diminution of the influence of the will on the muscles comes on with extreme slowness, is always accompanied, and even preceded, by agitations of the affected parts, and never by a lessened sense of feeling. The dictates of the will are even, in the last stages of the disease, conveyed to the muscles; and the muscles act on this impulse, but their actions are perverted.

Anomalous cases of convulsive affections (p. 29) have been designated by the term Shaking Palsy: a term which appears to be improperly applied to these cases, independent of the want of accordance between them and that disease which has been here denominated Shaking Palsy. Dr. Kirkland, in his commentary on Apoplectic and Paralytic Affections, &c. cites the following case, related by Dr. Charlton, as belonging, he says to the class of Shaking Palsies. "Mary Ford, of a sanguineous and robust constitution, had an involuntary motion of her right arm, occasioned by a fright, which first brought on convulsion fits, and most excruciating pain in the stomach, which vanished on a sudden, and her right arm was instantaneously flung into an involuntary and perpetual motion, like the swing of a pendulum, raising the hand, at every vibration higher than her head; but if by any means whatever it was stopped; the pain in her stomach came on again, and convulsion fits were the certain consequence, which went off when the vibration of her hand returned."

Another case, which the Doctor designates as "A Shaking Palsy," apparently from worms, he describes thus, "A poor boy, about (p. 30) twelve or thirteen years of age, was seized with a Shaking Palsy. His legs became useless, and together with his head and hands, were in continual agitation; after many weeks trial of various remedies, my assistance was desired.

"His bowels being cleared, I ordered him a grain of Opium a day in the gum pill; and in three or four days the shaking had nearly left him." By pursuing this plan, the medicine proving a vermifuge, he could soon walk, and was restored to perfect health.

Whether these cases should be classed under Shaking Palsy or not, is necessary to be here determined; since, if they are properly ranked, the cases which have been described in the preceding pages, differ so much from them as certainly to oppose their being classed together; and the disease, which is the subject of these pages, cannot be considered as the same with Shaking Palsy, as characterised by those cases.

The term Shaking Palsy is evidently inapplicable to the first of these cases, which (p. 31) appears to have belonged more properly to the genus *Convulsio*, of Cullen, or to *Hieranosos* of Linnæus and Vogel.*

The latter appears to be referable to that class of proteal forms of disease, generated by a disordered state of *primæ viæ*, sympathetically (p. 32) affecting the nervous influence in a distant part of the body.

* *Corporis agitatio continua, indolens, convulsiva, cum sensibilitate.*—Linn.

Agitatio corporis vel artuum convulsiva continua, chronica, cum integritate sensuum.—Vogel.

This genus is resolved by Cullen into that of *Convulsio*. Synops. Nosol. 1803.

Dr. Macbride has given a very interesting and illustrative case of this disease.

"*Hieranosos*, or *Morbus Sacer*, so called, as being vulgarly supposed to arise from witchcraft, or some extraordinary celestial influence, is a distinct genus of disease, though a very uncommon one; the author once had an opportunity of seeing a case. The patient was a lad about seventeen, who at that time had laboured under this extraordinary disease for more than twelve years. His body was so distorted, and the legs and arms so twisted round it, by the continued convulsive working, that no words can give an adequate idea of the oddity of his figure; the agitation of the muscles was perpetual; but in general he did not complain of pain nor sickness; and had his sense perfectly, insomuch that he used to assist his mother, who kept a little school, in teaching children to read." *A methodical Introduction to the Theory and Practice of Physic.* By David Macbride, M.D. p. 559.

Unless attention is paid to one circumstance, this disease will be confounded with those species of passive tremblings to which the term Shaking Palsies has frequently been applied. These are, tremor temulentus, the trembling consequent to indulgence in the drinking of spirituous liquors; that which proceeds from the immoderate employment of tea and coffee; that which appears to be dependent on advanced age; and all those tremblings which proceed from the various circumstances which induce a diminution of power in the nervous system. But by attending to that circumstance alone, which has been already noted as characteristic of mere tremor, the distinction will readily be made. If the trembling limb be supported, and none of its muscles be called into action, the trembling will cease. In the real Shaking Palsy the reverse of this takes place, the agitation continues in full force whilst the limb is at rest and unemployed; and even is sometimes diminished by calling the muscles into employment.

(p. 33) CHAP. IV. PROXIMATE CAUSE—REMOTE CAUSES—
ILLUSTRATIVE CASES

Before making the attempt to point out the nature and cause of this disease, it is necessary to plead, that it is made under very unfavourable circumstances. Unaided by previous inquiries immediately directed to this disease, and not having had the advantage, in a single case, of that light which anatomical examination yields, opinions and not facts can only be offered. Conjecture founded on analogy, and an attentive consideration of the peculiar symptoms of the disease, have been the only guides that could be obtained for this research, the result of which is, as it ought to be, offered with hesitation.

SUPPOSED PROXIMATE CAUSE

(A diseased state of the *medulla spinalis*, in that part which is contained in the canal, formed by the superior cervical (p. 34) vertebrae, and extending, as the disease proceeds, to the *medulla oblongata*)

By the nature of the symptoms we are taught, that the disease depends on some irregularity in the direction of the nervous

influence; by the wide range of parts which are affected, that the injury is rather in the source of this influence than merely in the nerves of the parts; by the situation of the parts whose actions are impaired, and the order in which they become affected, that the proximate cause of the disease is in the superior part of the medulla spinalis; and by the absence of any injury to the senses and to the intellect, that the morbid state does not extend to the encephalon.

Uncertainty existing as to the nature of the proximate cause of this disease, its remote causes must necessarily be referred to with indecision. Assuming however the state just mentioned as the proximate cause, it may be concluded that this may be the result of injuries of the medulla itself, or of the theca helping to form the canal in which it is inclosed.

(p. 35) The great degree of mobility in that portion of the spine which is formed by the superior cervical vertebrae, must render it, and the contained parts, liable to injury from sudden distortions. Hence therefore may proceed inflammation of quicker or of slower progress, disease of the vertebrae, derangement of structure in the medulla, or in its membranes, thickening or even ulceration of the theca, effusion of fluids, &c.

But in no case which has been noticed, has the patient recollected receiving any injury of this kind, or any fixed pain in early life in these parts, which might have led to the opinion that the foundation for this malady has been thus laid. On the subject indeed of remote causes, no satisfactory accounts has yet been obtained from any of the sufferers. Whilst one has attributed this affliction to indulgence in spirituous liquors, and another to long lying on the damp ground; the others have been unable to suggest any circumstance whatever, which, in their opinion, could be considered as having given origin, or disposed, to the calamity under which they suffered.

(p. 36) Cases illustrative of the nature and cause of this malady are very rare. In the following case symptoms very similar are observable, so far as affecting the lower extremities. That the medulla spinalis was here affected, and in its lower part, is not to be doubted: but this, unfortunately, was never

ascertained by examination. It must be however remarked, that this case differed from those which have been given of this disease, in the suddenness with which the symptoms appeared.

A. B. aged twenty-six years, during a course of mercury for a venereal affection, was exposed to severely inclement weather, for several hours, and the next morning, complained of extreme pain in the back, and of total inability to employ voluntarily the muscles of the lower extremities, which were continually agitated with severe convulsive motions. The physician who attended him employed those means which seemed best calculated to relieve him; but with no beneficial effect. The lower extremities were perpetually agitated with strong palpitatory motions, and, frequently, (p. 37) three or four times in a minute, suddenly raised with great vehemence two or three feet from the ground, either in a forward or oblique direction, striking one limb against the other, or against the chairs, tables, or any substance which stood in the way. To check these inordinate motions, no means were in the least effectual, except striking the thighs forcibly during the more violent convulsions. No advantage was derived from all the means which were employed during upwards of twelve months. Full ten years after this period, the unhappy subject of this malady was casually met in the street, shifting himself along, seated in a chair; the convulsive motions having ceased, and the limbs having become totally inert, and insensible to any impulse of the will.

It must be acknowledged, that in the well-known cases, described by Mr. Potts, of that kind of Palsy of the lower limbs which is frequently found to accompany a curvature of the spine, and in which a carious state of the vertebrae is found to exist, no instructive analogy is discoverable; slight convulsive motions may indeed (p. 38) happen in the disease proceeding from curvature of the spine; but palpitating motions of the limbs, such as belong to the disease here described, do not appear to have been hitherto noticed.

Whilst striving to determine the nature and origin of this disease, it becomes necessary to give the following particulars of an interesting case of Palsy occasioned by a fall, attended with un-

common symptoms, related by D. Maty, in the third volume of the Medical Observations and Inquiries. The subject of this case, the Count de Lordat, had the misfortune to be overturned from a pretty high and steep bank. His head pitched against the top of the coach, and was bent from left to right; his left shoulder, arm, and especially his hand, were considerably bruised. At first he felt a good deal of pain along the left side of his neck, but neither then, nor at any other time, had he any faintings, vomitings, or giddiness.—On the sixth day he was let blood, on account of the pain in his shoulder and the contusion of his hand, which were then the only symptoms he (p. 39) complained of, and of which he soon found himself relieved.—Towards the beginning of the following winter, he began to find *a small impediment in uttering some words, and his left arm appeared weaker*. In the following spring, having suffered considerably from the severities of the winter campaign, he found *the difficulty in speaking, and in moving his left arm, considerably increased*.—On employing the thermal waters of Bourbonne, his speech became freer, but, on his return to Paris, the Palsy was increased, and the arm somewhat wasted.—In the beginning of the next spring he went to Balaruc; when he became affected with *involuntary convulsive motions all over the body*. The left arm withered more and more, *a spitting began*, and now it was *with difficulty that he uttered a few words*. Frictions and sinapisms were successively tried, and an issue, made by a caustic, was kept open for some time without any effect; but no mention is made of what part the issue was established in.

Soon after this, and three years and a half after the fall, Doctor Maty first saw the patient, and gives the following description of (p. 40) his situation. “A more melancholy object I never beheld. The patient, naturally a handsome, middle-sized, sanguine man, of a cheerful disposition, and an active mind, appeared much emaciated, stooping, and dejected. *He still walked alone with a cane, from one room to the other, but with great difficulty, and in a tottering manner*; his left hand and arm were much reduced, and would hardly perform any motion; *the right was somewhat benumbed, and he could scarcely lift it up to*

his head; his saliva was continually trickling out of his mouth, and he had neither the power of retaining it, nor of spitting it out freely. What words he still could utter were monosyllables, and these came out, after much struggle, in a violent expiration, and with such a low voice and indistinct articulation, as hardly to be understood but by those who were constantly with him. He fetched his breath rather hard; his pulse was low, but neither accelerated nor intermitting. He took very little nourishment, could chew and swallow no solids, and even found great pain in getting down liquids. Milk was almost his only food; his body was rather loose, his urine (p. 41) natural, his sleep good, his senses, and the powers of his mind, unimpaired; he was attentive to, and sensible of every thing which was said in conversation, and shewed himself very desirous of joining in it; but was continually checked by the impediment in his speech, and the difficulty which his hearers were put to. Happily for him he was able to read, and as capable as ever of writing, as he shewed me, by putting into my hands an account of his present situation, drawn up by himself: and I am informed that he spent his time to the very last, in writing upon some of the most abstruse subjects."

This gentleman died about four years after the accident, when the body was examined by Dr. Bellett and Mons. Sorbier, who made the following report:

"We first examined the muscles of the tongue, which were found extenuated and of a loose texture. We observed no signs of compression in the lingual and brachial nerves, as high as their exit from the basis of the cranium and the vertebrae of the neck; (p. 42) but they appeared to us more compact than they commonly are; being nearly tendinous. The dura mater was in a sound state, but the pia mater was full of blood and lymph; on it several hydatids, and towards the falx some marks of suppuration were observed. The ventricles were filled with water, and the plexus choroides were considerably enlarged, and stuffed with grumoun blood. The cortical surface of the brain appeared much browner than usual, but neither the medullary part nor cerebellum were impaired. We chiefly took notice of

the Medulla Oblongata, this was greatly enlarged, surpassing the usual size by more than one third. It was likewise more compact. The membranes, which, in their continuation, inclose the spinal marrow, were so tough that we found great difficulty in cutting through them, and we observed this to be the cause of the tendinous texture of the cervical nerves. The marrow itself had acquired such solidity as to elude the pressure of our fingers, it resisted as a callous body, and could not be bruised. This hardness was observed all along the vertebrae of the neck, but lessened by degrees, and (p. 43) was not near so considerable in the vertebrae of the thorax. Though the patient was but nine and thirty years old, the cartilages of the sternum were ossified, and required as much labour to cut them asunder as the ribs; like these they were spungy, but somewhat whiter. The lungs and heart were sound. At the bottom of the stomach appeared an inflammation, which increased as it extended to the intestines. The ileum looked of that dark and livid hue, which is observed in membranous parts tending to mortification. The colon was not above an inch in diameter, the rectum was smaller still, but both appeared sound.—From these appearances, we were at no loss to fix the cause of this gradual palsy in the alteration of the medulla spinalis and oblongata.”

Dr. Bellett offers the following explanation of these changes. “I conceive, that, by this accident, the head being violently bent to the right, the nervous membranes on the left were excessively stretched and irritated; that this cause extended by degrees to the spinal marrow, which being (p. 44) thereby compressed, brought on the paralytic symptoms, not only of the left arm, but at last in some measure also of the right. This induration seems to have been occasioned by the constant afflux of the nutritive juices, which were stopt at that place, and deprived of their most liquid parts; the grosser ones being unable to spread in the bony cavity, by which they were confined, could only acquire a greater solidity, and change a soft body into a hard and nearly osseous mass. This likewise accounts for the increase of the medulla oblongata, which being loaded with more juices than it could send off, swelled in the same

manner as the branches of trees, which will grow of a monstrous size, when the sap that runs into them is stopt in its progress. The medulla oblongata not growing so hard as the spinalis, was doubtless owing to its not being confined in an osseous theca, but surrounded with soft parts, which allowed it room to spread. The obstruction from the bulk of this substance must have affected the brain, and probably induced the thickening of the pia mater, the hydatids, and the beginning of suppuration, whereas the dura (p. 45) mater being of a harder texture, was not injured.*"

In some of the symptoms which appeared in this case, an agreement is observable between it and those cases which are mentioned in the beginning of these pages. The weakened state of both arms; the power first lessening in one arm, and then in a similar manner in the other arm; the affection of the speech; the difficulty in chewing and in swallowing; as well as of retaining, or freely discharging, the spittle; the convulsive motions of the body; and the unimpaired state of the intellects; constitute such a degree of accordance as, although it may not mark an identity of disease, serves at least to show that nearly the same parts were the seat of the disease, in both instances. Thus we attain something like confirmation of the supposed proximate cause, and of one of the assumed occasional causes.

Whilst conjecturing as to the cause of this disease, the following collected observations (p. 46) on the effects of injury to the medulla spinalis, by Sir Everard Home, become particularly deserving of attention. It thence appears, that none of the characteristic symptoms of this malady are produced by compression, laceration, or complete division of the medulla spinalis.

"Pressure upon the medulla spinalis of the neck, by coagulated blood, produced paralytic affections of the arm and legs; all the functions of the internal organs were carried on for thirty-five days, but the urine and stools passed involuntarily.†

* Medical Observations and Inquiries, Vol. III. p. 257.

† A coagulum of blood, the thickness of a crown-piece, was found lying upon the external surface of the dura-matral covering of the medulla spinalis, extending from the fourth vertebra colli to the second vertebra dorsi. The medulla spinalis itself was uninjured.

"Blood extravasated in the central part of the medulla, in the neck, was attended with paralytic affection of the legs, but not of the arms*.

(p. 47) "In a case where the substance of the medulla was lacerated in the neck, there was a paralysis in all the parts below the laceration, the lining of the oesophagus was so sensible, that solids could not be swallowed, on account of the pain they occasioned.†

"When the medulla of the back was completely divided, there was momentary loss of sight, loss of memory for fifteen minutes, and permanent insensibility in all the lower parts of the body. The skin above the division of the spinal marrow perspired, that below did not. The wounded spinal marrow appeared to be extremely sensible‡." *Philosophical Transactions* 1816, p. 485.

In two of the cases already noticed, symptoms of rheumatism had previously existed; and in Case IV. the right arm, in which the palpitation began, was said to (p. 48) have been very violently affected with rheumatic pain to the finger ends. The consideration of this case, in which the palpitation had been preceded, at a considerable distance of time, by this painful affection of the arm, led to the supposition that this latter circumstance might be the cause of the palpitations, and the other subsequent symptoms of this disease. This supposition naturally occasioned the attention to be eagerly fixed on the following case; and of course influenced the mode of treatment which was adopted.

A. B. subject to rheumatic affection of the deltoid muscle, had felt the usual inconveniences from it for two or three days; but at night found the pain had extended down the arm, along the inside of the fore-arm, and on the sides of the fingers, in which a continual tingling was felt. The pain, without being extremely

* The sixth and seventh vertebra colli were dislocated, the medulla spinalis, externally, was uninjured; but in the centre of its substance, just at that part, there was a coagulum of blood nearly two inches in length.

† The seventh vertebra colli was fractured, and the medulla spinalis passing through it, was lacerated and compressed.

‡ The spinal marrow, within the canal of the sixth vertebra dorsi, was completely destroyed by a musket ball. The person lived four days.

intense, was such as effectually to prevent sleep: and seemed to follow the course of the brachial nerve. Whilst ascertaining the propriety of this conclusion, the pain was found to ramify, as it were, on the fore and back part of the (p. 49) chest; and was slightly augmented by drawing a deep breath.

These circumstances suggested the probability of slight inflammation, or increased determination to the origin of the nerves of these parts, and to the neighbouring medulla. On this ground, blood was taken from the back part of the neck, by cupping; hot fomentations were applied for about the space of an hour, when the upper part of the back of the neck was covered with a blister, perspiration was freely induced by two or three small doses of antimonials, and the following morning the bowels were evacuated by an appropriate dose of calomel. On the following day the pains were much diminished, and in the course of four or five days were quite removed. The arm and hand felt now more than ordinarily heavy, and were evidently much weakened: aching, and feeling extremely wearied after the least exertion. The strength of the arm was not completely recovered at the end of more than twelvemonths; and, after more than twice that time, exertion would excite the feeling of painful weariness, but no palpitation (p. 50) or other unpleasant symptom has occurred during the five or six years which have since passed.

The commencement, progress, and termination of this attack; with the success attending the mode of treatment, and the symptoms which followed, seem to lead to the conjecture, that the proximate cause of the disease, in this case, existed in the medulla spinalis, and that it might, if neglected, have gradually resolved itself into that disease which is the object of our present inquiry.

Some few months after the occurrence of the preceding case, the writer of these lines was called to a female about forty years of age, complaining of great pain in both the arms, extending from the shoulder to the finger ends. She stated, that she was attacked in the same manner as is described in the preceding case, about nine months before; that the complaint was considered as

rheumatism, and was not benefited by any of the medicines which had been employed; but that after three or four weeks (p. 51) it gradually amended, leaving both the arms and hands in a very weakened and trembling state. From this state they were now somewhat recovered; but she was extremely anxious, fearing that if the present attack should not be soon checked, she might entirely lose the use of her hands and arms.

Instructed by the preceding case, similar means were here recommended. Leeches, stimulating fomentations, and a blister, which was made for sometime to yield a purulent discharge, were applied over the cervical vertebrae; and in the course of a very few days the pain was entirely removed. It is regretted that no farther information, as to the progress of this case, could be obtained.

On meeting with these two cases, it was thought that it might not be improbable that attacks of this kind, considered at the time merely as rheumatic affections, might lay the foundation of this lamentable disease, which might manifest itself at some distant period, when the circumstance in which it had originated, had, perhaps, almost escaped (p. 52) the memory. Indeed when it is considered that neither in the ordinary cases of Palsy of the lower extremities, proceeding from diseased spine, nor in cases of injured medulla from fractured vertebrae, any of the peculiar symptoms of this disease are observable, we necessarily doubt as to the probability of its being the direct effect of any sudden injury. But taking all circumstances into due consideration, particularly the very gradual manner in which the disease commences, and proceeds in its attacks; as well as the inability to ascribe its origin to any more obvious cause, we are led to seek for it in some slow morbid change in the structure of the medulla, or its investing membranes, or theca, occasioned by simple inflammation, or rheumatic or scrophulous affection.

It must be too obvious that the evidence adduced as to the nature of the proximate and occasional causes of this disease, is by no means conclusive. A reference to the test therefore which will be yielded by an examination of some of the more prominent symptoms, especially as to their agreement (p. 53)

with the supposed proximate cause, is more particularly demanded. Satisfied as to the importance of this part of the present undertaking, no apology is offered for the extent to which the examination is carried on.

If the palpitation and the attendant weakness of the limbs, &c. be considered as to the order in which the several parts are attacked, it is believed, that some confirmation will be obtained of the opinion which has been just offered, respecting the cause, or at least the seat, of that change which may be considered as the proximate cause of this disease.

One of the arms, in all the cases which have been here mentioned, has been the part in which these symptoms have been first noticed; the legs, head, and trunk have then become gradually affected, and lastly, the muscles of the mouth and fauces have yielded to the morbid influence.

The arms, the parts first manifesting disordered action, of course direct us, whilst (p. 54) searching for the cause of these changes, to the brachial nerves. But finding the mischief extending to other parts, not supplied with these, but with other nerves derived from nearly the same part of the medulla spinalis, we are of course led to consider that portion of the medulla spinalis itself, from which these nerves are derived, as the part in which those changes have taken place, which constitute the proximate cause of this disease.

From the subsequent affection of the lower extremities, and from the failure of power in the muscles of the trunk, such a change in the substance of the medulla spinalis may be inferred, as shall have considerably interrupted, and interfered with, the extension of the nervous influence to those parts, whose nerves are derived from any portion of the medulla below the part which has undergone the diseased change.

The difficulty in supporting the trunk erect, as well as the propensity to the adopting of a hurried pace, is also referable to such a diminution of the nervous power in (p. 55) the extensor muscles of the head and trunk, as prevents them from performing the offices of maintaining the head and body in an erect position.

From the impediment to speech, the difficulty in mastication and swallowing, the inability to retain, or freely to eject, the Saliva, may with propriety be inferred an extension of the morbid change upwards through the medulla spinalis to the medulla oblongata, necessarily impairing the powers of the several nerves derived from that portion into which the morbid change may have reached. In the late occurrence of this set of symptoms, and the extension upwards of the diseased state, a very close agreement is observable between this disease and that which has been already shown, proved fatal to the Count de Lordat. But in this case, the disease doubtlessly became differently modified, and its symptoms considerably accelerated, in consequence of the magnitude of the injury by which the disease was induced.

(p. 56) CHAP. V. CONSIDERATIONS RESPECTING THE MEANS
OF CURE

The inquiries made in the preceding pages yield, it is to be much regretted, but little more than evidence of inference; nothing direct and satisfactory has been obtained. All that has been ventured to assume here, has been that the disease depends on a disordered state of that part of the medulla which is contained in the cervical vertebrae. But of what nature that morbid change is; and whether originating in the medulla itself, in its membranes, or in the containing theca, is, at present, the subject of doubt and conjecture. But although, at present, uninformed as to the precise nature of the disease, still it ought not be considered as one against which there exists no counter-vailing remedy.

On the contrary, there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least, the progress of the disease may be (p. 57) stopped. It seldom happens that the agitation extends beyond the arms within the first two years; which period, therefore, if we were disposed to divide the disease into stages, might be said to comprise the first stage. In this period, it is very probable,

that remedial means might be employed with success: and even, if unfortunately deferred to a later period, they might then arrest the farther progress of the disease, although the removing of the effects already produced, might be hardly to be expected.

From a review of the changes which had taken place in the case of Count de Lordat, it seems as if we were able to trace the order and mode in which the morbid changes may proceed in this disease. From any occasional cause, the thecal ligament, the membranes, or the medulla itself, may pass into the state of simple excitement or irritation, which may be gradually succeeded by such a local afflux and determination of blood into the minute vessels, as may terminate in actual but slow inflammation. The result of this would be a thickening (p. 58) of the theca, or membranes, and perhaps an increase in the volume of the medulla itself, which would gradually occasion such a degree of pressure against the sides of the unyielding canal, as must eventually intercept the influence of the brain upon the inferior portion of the medullary column, and upon the parts on which the nerves of this portion are disposed.

From this review, and assuming that the morbid changes in this disease may not be widely dissimilar from those which occurred in the case of Count de Lordat, the chance of relief from the proposed mode of treatment may appear to be sufficient to warrant its trial.

In such a case then, at whatever period of the disease it might be proposed to attempt the cure, blood should be first taken from the upper part of the neck, unless contra-indicated by any particular circumstance. After which vesicatories should be applied to the same part, and a purulent discharge obtained by appropriate use of the Sabine Liniment; having recourse to (p. 59) the application of a fresh blister, when from the diminution of the discharging surface, pus is not secreted in a sufficient quantity. Should the blisters be found too inconvenient, or a sufficient quantity of discharge not be obtained thereby, an issue of at least an inch and a half in length might be established on each side of the vertebral columna, in its superior part. These, it is

presumed, would be best formed with caustic, and kept open with any proper substance*.

Could it have been imagined that such considerable benefit: indeed, that such astonishing cures, could have been effected by issues in cases of Palsy of the lower extremities from diseased spine? although satisfied with ascribing those cases to scrofulous action, we are in fact as little informed respecting the nature of the affection, inducing (p. 60) the carious state of the vertebrae, as we are respecting the peculiar change of structure which takes place in this disease. Equally uninformed are we also as to the peculiar kind of morbid action, which takes place in the ligaments of the joints; as well as that which takes place in different instances of deep seated pains and affections of the parts contained in the head, thorax, and abdomen, and in all which cases the inducing of a purulent discharge in their neighbourhood is so frequently productive of a cure. Experiment has not indeed been yet employed to prove, but analogy certainly warrants the hope, that similar advantages might be derived from the use of the means enumerated, in the present disease. It is obvious, that the chance of obtaining relief will depend in a great measure on the period at which the means are employed. As in every other disease, so here, the earlier the remedies are resorted to, the greater will be the probability of success. But in this disease there is one circumstance which demands particular attention; the long period to which it may be extended. One of its peculiar symptoms, *Scelotyrbe festinans*, may (p. 61) not occur until the disease has existed ten or twelve years, or more; hence, when looking for the period, within which our hopes of remedial aid is to be limited; we may, guided by the slow progress of the malady, extend it to a great length, when compared with that within which we should be obliged to confine ourselves in most other diseases.

* Cork, which has been hitherto neglected, appears to be very appropriate to this purpose. It possesses lightness, softness, elasticity and sufficient firmness; and also capable of being readily fashioned to any convenient form. The form which it seems would be best adapted to the part, is that of an almond, or of the variety of bean called scarlet bean; but at least an inch and a half in length.

But it is much to be apprehended, as in many other cases, that the resolution of the patients will seldom be sufficient to enable them to persevere through the length of time which the proposed process will necessarily require. As slow as is the progress of the disease, so slow in all probability must be the period of the return to health. In most cases, especially in those in which the disease has been allowed to exist long unopposed, it may be found that all that art is capable of accomplishing, is that of checking its further progress. Nor will this be regarded as a trifle, when, by reference to the history of the disease, is seen the train of harassing evils which would be thus avoided.

(p. 62) But it seems as if there existed reason for hoping for more. For supposing change of structure to have taken place, it is extremely probable that this change may be merely increase in mass or volume by interstitial addition, the consequence of increased action in the minute vessels of the part. In that case, should the instituting of a purulent discharge, in a neighbouring part, act in the manner which we would presume it may—should it by keeping up a constant discharge, not merely alter the determination, but diminish the inordinate action of the vessels in the diseased part; and at the same time excite the absorbents to such increased action as may remove the added matter; there will exist strong ground for hope, that a happy, though slow restoration to health, may be obtained.

Until we are better informed respecting the nature of this disease, the employment of internal medicines is scarcely warrantable; unless analogy should point out some remedy the trial of which rational hope might authorize. Particular circumstances indeed (p. 63) must arise in different cases, in which the aid of medicine may be demanded: and the intelligent will never fail to avail themselves of any opportunity of making trial of the influence of mercury, which has in so many instances, manifested its power in correcting derangement of structure.

The weakened powers of the muscles in the affected parts is so prominent a symptom, as to be very liable to mislead the inattentive, who may regard the disease as a mere consequence of constitutional debility. If this notion be pursued, and tonic

medicines, and highly nutritious diet be directed, no benefit is likely to be thus obtained; since the disease depends not on general weakness, but merely on the interruption of the flow of the nervous influence to the affected parts.

It is indeed much to be regretted that this malady is generally regarded by the sufferers in this point of view, so discouraging to the employment of remedial means. Seldom occurring before the age of fifty, and frequently yielding but little inconvenience (p. 64) for several months, it is generally considered as the irremediable diminution of the nervous influence, naturally resulting from declining life; and remedies therefore are seldom sought for.

Although unable to trace the connection by which a disordered state of the stomach and bowels may induce a morbid action in a part of the medulla spinalis, yet taught by the instruction of Mr. Abernethy, little hesitation need be employed before we determine on the probability of such occurrence. The power, possessed by sympathy, of inducing such disordered action in a distant part, and the probability of such disordered action producing derangement of structure, can hardly be denied. The following Case seems to prove, at least, that the mysterious sympathetic influence which so closely simulates the forms of other diseases, may induce such symptoms as would seem to menace the formation of a disease not unlike to that which we have been here treating of.

A. B. A man, 54 years of age, of temperate (p. 65) habits and regular state of bowels, became gradually affected with slight numbness and prickling, with a feeling of weakness in in both arms, accompanied by a sense of fulness about the shoulders, as if produced by the pressure of a strong ligature; and at times a slight trembling of the hands. During the night, the fullness, numbness, and prickling were much increased. The appetite had been diminished for several weeks; and the abdomen, on being examined, felt as though containing considerable accumulation.

Before adopting any other measures, and as there appeared to be no marks of vascular fulness, it was determined to empty the

bowels. This was done effectually by moderate doses of calomel, with the occasional help of Epsom salts; and in about ten days, by these means alone, the complaints were entirely removed.

Before concluding these pages, it may be proper to observe once more, that an important object proposed to be obtained by them is, the leading of the attention of (p. 66) those who humanely employ anatomical examination in detecting the causes and nature of diseases, particularly to this malady. By their benevolent labours its real nature may be ascertained, and appropriate modes, of relief, or even of cure, pointed out.

To such researches the healing art is already much indebted for the enlargement of its powers of lessening the evils of suffering humanity. Little is the public aware of the obligations it owes to those who, led by professional ardour, and the dictates of duty, have devoted themselves to these pursuits, under circumstances most unpleasant and forbidding. Every person of consideration and feeling, may judge of the advantages yielded by the philanthropic exertions of a HOWARD; but how few can estimate the benefits bestowed on mankind, by the labours of a MORGAGNI, HUNTER, or BAILLIE.

Finis



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